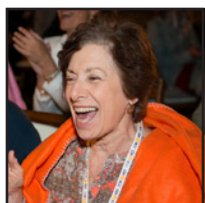


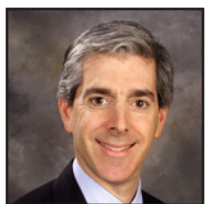
June 2014

NIEHS Spotlight



[Birnbaum receives honorary doctorate from Ben-Gurion University](#) Video

NIEHS and NTP Director Linda Birnbaum, Ph.D., added one more laurel to her long list May 20 with the award of an honorary doctorate by Ben-Gurion University.



[National Climate Assessment includes key messages about human health](#)

Released May 6, the NCA makes clear that climate change, once thought an issue for the distant future, has moved firmly into the present, with impacts on human health.



[Centers of excellence program adds Texas consortium](#)

NIEHS has designated the new Center for Translational Environmental Health Research in Texas as one of the newest National Center of Excellence in Environmental Health Science.



[Director of FNIH promotes foundation](#)

Foundation for NIH director Maria Freire, Ph.D., seeks to change the lack of FNIH support for NIEHS research.

Science Notebook



[Kunkel elected to American Academy of Arts and Sciences](#) Video

This fall, NIH distinguished lead researcher Thomas Kunkel, Ph.D., will join fellow members in the 2014 class of the American Academy of Arts and Sciences.



[Understanding organ development](#)

At a May 6 NIEHS distinguished lecture, Christopher Wright, D.Phil., discussed his work on pancreas development, with implications for cell-based disease therapy.



[Peer review panel evaluates draft NTP technical reports](#)

The NTP peer review panel met May 22 to review draft technical reports on two dietary supplements, a water disinfection byproduct, and a metalworking fluid.



[Statistical geneticist Dmitri Zaykin tenured](#)

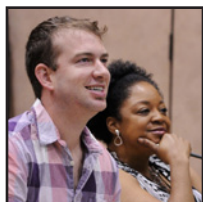
NIH Central Tenure Committee awards tenure to NIEHS statistical geneticist Dmitri Zaykin, Ph.D., who works at the interface of mathematics, statistics, and biology.

NIEHS Spotlight



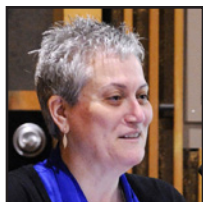
[Pregnant and breastfeeding women need iodine supplements](#)

New policy statement from the American Academy of Pediatrics aims to protect children from iodine deficiency and adverse impacts of certain environmental chemicals.



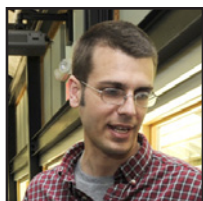
[Event helps employees laugh their way into ethical compliance](#)

NIEHS held its fifth annual Ethics Day May 15 with a refreshing mix of tunes, funny yet instructional videos, good-natured competition, and serious talk about ethical conduct.



[Variety of topics covered at council](#)

At the 142nd meeting of the National Advisory Environmental Health Sciences Council, members learned about NIEHS programs and provided thoughtful feedback.



[Molecular genetics groups break for annual retreat](#)

The NIEHS Laboratory of Molecular Genetics kicked off its two-day departmental retreat May 8 at the North Carolina Botanical Garden in Chapel Hill, North Carolina.



[Genomics Day highlights breadth of NIEHS resources and research](#)

The fifth annual Genomics Day highlighted genomics resources available to NIEHS researchers and featured posters and talks on the research those resources support.

Science Notebook



[Small fish may offer big opportunities for future toxicity testing](#)

An international gathering of researchers, co-sponsored by NTP and NCSU, explored the role aquatic species may play in new approaches to toxicity testing.



[Cell signaling researcher explores the frontiers of therapeutic potential](#)

NIEHS lead researcher Stephen Shears, Ph.D., opened his May 12 talk at NIEHS on inositol pyrophosphate signaling by describing its title as provocative.



[Fast test for measuring DNA repair](#)

NIEHS-funded researchers at MIT report that a new test for DNA repair capacity may help doctors predict cancer risk and patient response to chemotherapy drugs.



[Scientists study impacts of climate change on public health](#)

NIEHS-funded scientists developing methods to assess and quantify the role of climate change on human health presented their work at an April 25 webinar.



[Prenatal arsenic exposure and altered protein expression](#)

NIEHS-funded researchers found prenatal arsenic exposure altered expression of 111 proteins and was associated with decreased head circumference of newborn males.

NIEHS Spotlight



[NIEHS Biomedical Career Symposium draws hundreds](#)

Nearly 400 people attended the daylong event featuring workshops, networking, and job-hunting advice on a variety of career paths.



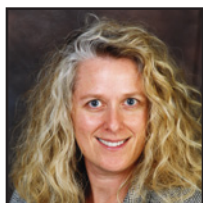
[Emerging concerns with PCBs in schools draw hundreds to SRP webinars](#)

Two April webinars provided more than 300 people with overview, exposure assessment, and approaches to reducing health risks from PCBs in schools.



[NIEHS reaches out at nation's largest STEM event](#)

Members of the NIEHS Office of Science Education and Diversity were part of a trans-NIH effort at the 2014 USA Science and Engineering Festival April 26-27.



[Translating research into products to improve public health](#)

Three NIEHS-funded researchers, who have launched start-ups that promise to enhance public health, were recognized for their efforts this spring.



[NIEHS fellows earn honors at NIH Postbac Poster Day](#)

Caitlin McDonough and Jessica Boni won Outstanding Poster awards May 1 at the 2014 Postbac Poster Day at the NIH main campus in Bethesda, Maryland.

Science Notebook



[High-throughput toxicity screening produces human-relevant results](#)

Tox21 scientists report in the journal Nature Biotechnology a human-relevant system to provide rapid and accurate toxicity screening.



[Investigating medications as a source of phthalate exposure](#)

Epidemiologist Sonia Hernandez-Diaz, M.D., Dr.P.H. shared the evolution of her studies of potential phthalate exposure in medications during a talk May 12 at NIEHS.



[New exposure biomarkers enhance breast cancer research](#)

Scientists at the NIEHS-funded Silent Spring Institute have established new biomarkers for exposure to chemicals of interest to breast cancer researchers.



[Novel integrative approach sheds light on embryonic stem cell identity](#)

NIEHS scientists find previously unknown regulatory circuitry, with potentially profound implications for understanding cell fate decisions in cancer stem cells.



[Yao receives award and helps launch new center](#)

NIEHS lead researcher Humphrey Yao, Ph.D., was in Denmark last month, helping launch a new research center and delivering presentations at the 18th European Testis Workshop.

Inside the Institute



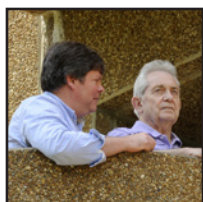
[Administrative professionals recharge and empower at NIEHS seminar](#)

NIEHS support staff gathered April 23 for a lively workshop on strategies for recognizing accomplishments, managing stress, and establishing respect.



[NIEHS renovation team wins HHS Green Champions Award](#)

The Green and Fit Retrofit team was selected for a small group award, for the sustainable, healthy priorities that guided a recent NIEHS renovation.



[Lead design architect revisits NIEHS](#)

More than three decades after completion of the main building at NIEHS, lead design architect Richard Banks returned to NIEHS May 19 for the first time.



[Fun and fitness abound during 2014 NIEHS Health and Fitness Week](#)

May 5 marked the beginning of NIEHS Health and Fitness Week, an unofficial rite of spring, with multiple events every day of the week.

Science Notebook



[This month in EHP](#)

The June issue of Environmental Health Perspectives examines potentially harmful exposures from cooking, and the benefits seen in Denmark from reduced antibiotic use in livestock.

Extramural Research

[Extramural papers of the month](#)

- [Olestra reduces PCBs in the body](#)
- [Activation and regulation of polymerase V during DNA synthesis](#)
- [SSRI use during pregnancy associated with autism](#)
- [Coal-burning stoves in Mongolia linked to seasonal variance in miscarriages](#)

Intramural Research

[Intramural papers of the month](#)

- [NTP researchers find potential treatment for damaged salivary glands is safe and effective](#)
- [Human obesity increases colon cancer risk](#)
- [New computational approach identifies essential stem cell genes](#)
- [p53 and NF-kappaB work together to promote inflammation](#)
- [More evidence for smoking-related changes in DNA methylation](#)

Calendar of Upcoming Events

- **June 3**, in the Executive Conference Room, noon-1:00 p.m. — Receptor Mechanisms Discussion Group Seminar Series, featuring Carolyn Mattingly, Ph.D., addressing “Predicting Chemical-Gene-Disease Interactions with CTD [Comparative Toxicogenomics Database]”
- **June 4**, webinar, 3:00-4:30 p.m. — NIEHS Superfund Research Program Arsenic Panel Discussion Webinar Series, “Part 4: Prevention and Remediation Strategies for Arsenic Exposure,” [register](#)
- **June 5**, in Rall D350, 11:00 a.m.-noon — Laboratory of Toxicology and Pharmacology Seminar Series explores “Early Antidepressant Exposure Induces Global Network and Glial Dysfunctions,” by Rick Lin, Ph.D.
- **June 9**, in Keystone 1003AB, 11:00 a.m.-noon — Keystone Science Lecture Series, with Leo Trasande, M.D., presenting “The Economic Case for Protecting the Public from Environmental Hazards”
- **June 10**, [webcast](#) from Bethesda, Maryland, 10:00-11:30 a.m. — NIH Office of Equity, Diversity, and Inclusion LGBTI Portfolio presentation, “On Being Human: Reflections on Trans* Health and Wellness,” with panelists Cecilia Chung, Ruby Corado, Rayceen Pendarvis, and JV Sapinoso, Ph.D.
- **June 12 (offsite event)**, in the Daily Planet Cafe at the North Carolina Museum of Natural Sciences in Raleigh, North Carolina, 7:00-9:00 p.m. — Science Café discussion of “History and Roles of the U.S. Public Health Service Commissioned Corps,” with Capt. Terri Clark, D.V.M.
- **June 17-18**, in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — NTP Board of Scientific Counselors meeting
- **June 18**, [webcast](#) from Bethesda, Maryland, 3:00-4:00 p.m. — NIH Wednesday Afternoon Lecture Series, featuring a presentation by Donald Ingber, M.D., Ph.D., “Human Organs on Chips and Programmable Nanotherapeutics”
- **June 21-24 (offsite event)**, at McCormick Place West in Chicago, 8:30 a.m.-5:00 p.m. — Endocrine Society annual meeting
- **June 24 (offsite event)**, at the NIH William H. Natcher Conference Center in Bethesda, Maryland, 1:00-4:00 p.m. — ICCVAM Public Forum, [register](#) by June 11
- **June 30-July 2**, in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — Outstanding New Environmental Scientists (ONES) awardee meeting
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Birnbaum receives honorary doctorate from Ben-Gurion University

By Eddy Ball

NIEHS and NTP Director Linda Birnbaum, Ph.D., added one more laurel to her long list May 20 with the award of an honorary doctorate by Ben-Gurion University (BGU) of the Negev in Beer-Sheva, Israel. Each year, the university recognizes a select group of outstanding scholars, artists, and philanthropists, during its annual board of directors meeting.

In her award letter to Birnbaum, BGU President Rivka Carmi, M.D., described the honor. “The criteria we adhere to specify that honorary degrees may be awarded to individuals of real achievement and eminence in their respective fields, individuals who are distinguished by excellence, originality, and the capacity to excite,” she wrote.

For Birnbaum, returning to Beer-Sheva brought back memories of her trip there not long after the university was established. “The first time I visited in 1977, it was a dusty, desert outpost,” she said. “Now it’s truly an oasis — a center of learning in many fields with a strong scientific emphasis.”

An environmentally conscious university

Founded in 1969 as the University of the Negev, and renamed for Israel’s first prime minister, David Ben-Gurion, after his death in 1973, BGU is a leading Israeli university with several programs ranked, academically, among the world’s top 100. BGU prides itself on advanced research and applications at the forefront of science and technology, with strong interdisciplinary emphasis, a green campus and world-class sustainability program, community involvement, and local development.

Along with its North American-style medical school, BGU is home to national and multidisciplinary research institutes, including the National Institute for Biotechnology in the Negev, S. Daniel Abraham International Center for Health and Nutrition, and National Solar Energy Center.



Birnbaum, center, received her diploma from Carmi, as BGU Rector Zvi HaCohen, Ph.D., looked on. (Photo courtesy of BGU)



The tone of the board meeting changed dramatically after the pomp and circumstance of awarding diplomas. Birnbaum, right, made new friends with fellow musicians. (Photo courtesy of BGU)

The latest of many awards and honors

This year, Birnbaum joined seven other [awardees](#) in the ceremony on the BGU Marcus Family Campus. The other awardees included Nobel laureate and cancer researcher Linda Buck, Ph.D.; Pulitzer Prize and Israel Prize winning Holocaust historian Saul Friedlander, Ph.D.; Oxford University Vice Chancellor Andrew Hamilton, Ph.D.; acclaimed classical pianist Evgeny Kissin; and philanthropists James Breslauer, Nahum Guzik, and Cheryl Saban, Ph.D.



Also honored during the board meeting was Shimon Peres, president of the State of Israel, who received the Ben-Gurion Leadership Award and presented his last speech as president.

In addition to her honorary degree from BGU, Birnbaum has been honored by the Institute of Medicine of the National Academies, Collegium Ramazzini, University of Rochester, University of Illinois at Urbana-Champaign, Society of Toxicology, National Center for Women, Breast Cancer Fund, American Public Health Association, National Institutes of Health, and the U.S. Environmental Protection Agency, among others.

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National Climate Assessment includes key messages about human health

By Paula Whitacre

The U.S. Global Change Research Program (GCRP), comprising 13 federal agencies, released its Third National Climate Assessment (NCA) May 6, with the message that climate change, once considered an issue for the distant future, has moved firmly into the present, with impacts on human health. NIEHS was an active player in developing the health-related aspects of the assessment and continues to provide technical input and support in follow-through activities.

Different from previous assessments

A 60-member federal advisory committee and more than 300 experts produced the NCA, which looks at climate change in the U.S. across sectors, such as agriculture, energy, and health, as well as geographic regions. “The real importance of this NCA report, compared to the previous two, is that it is very much oriented to the general public,” said John Balbus, M.D., NIEHS senior advisor for public health, who was a lead author for the human health chapter. “People are much more engaged than with previous assessments,” he said.



His role with the NCA is only one of the NIEHS efforts on climate change that Balbus oversees. (Photo courtesy of Steve McCaw)

Kimberly Thigpen Tart, J.D., program analyst in NIEHS Office of Policy, Planning, and Evaluation, was involved in agency review and dissemination of the NCA. “This assessment focused on creating more than just another document,” she said. “We also developed an ongoing, sustainable process for looking at climate change impacts across the country.”

Balbus wins HHS Green Champion Award

The Department of Health and Human Services (HHS) selected Balbus for the Good Neighbor Award for his work developing the Sustainable and Climate Resilient Healthcare Facilities Initiative, as part of the President's Climate Action Plan, released in June 2013.

The Good Neighbor Award is one of the annual HHS Green Champion awards (see [related story](#)), which recognize efforts that support sustainability and climate resilience. Combined with his leadership role on the health effects portion of the NCA, this award demonstrates that Balbus is sincere and proactive when it comes to responding to climate change.

"In developing the Sustainable and Climate Resilient Healthcare Facilities Initiative, Dr. Balbus identified an urgent need for hospitals and other health care facilities to prepare for and adapt to global climate change," states the award, in part.

Congratulations, and a hearty thanks for helping healthcare facilities be prepared for the consequences of global climate change.

As part of the strategy to reach a more general audience, the GCRP [website](#), noted Balbus, is deliberately visual and interactive, with graphics and short summaries of key points (see example below). The report received extensive media attention, from front pages of newspapers to lead stories on evening newscasts, and as a trending topic on Twitter. Moreover, the coverage often emphasized health, such as the effects of climate change on allergens, asthma, and vector-borne diseases.

Health in the NCA

The chapter on health includes four key messages related to human health (see [text box](#)) and discusses existing and emerging threats, as well as the potential for reducing the severity of future climate change. Such reduction would provide immediate health benefits.

Health was covered in the 2000 and 2009 assessments, but in the current assessment, the role of NIEHS in providing subject matter expertise has been expanded, according to Balbus. NIEHS developed a literature database to assist the authors of the health chapter. In addition, the Interagency Crosscutting Group on Climate Change and Human Health, which NIEHS co-chairs, supported workshops in the northwestern and southeastern U.S. that provided technical input.

NIEHS supports research, and contributes scientific information, to policy [activities](#) related to climate change and human health. The Institute is also actively engaged in an interim assessment on climate change and human health. Balbus expects that this effort to include quantitative assessments on health impacts will rely in part on the work of NIEHS grantees (see [story](#)).



Thigpen Tart, along with Balbus, is an NIEHS contact for the NCA, and supports NIEHS global environmental health activities, a theme of the Institute's 2012-2017 [Strategic Plan](#). (Photo courtesy of Steve McCaw)

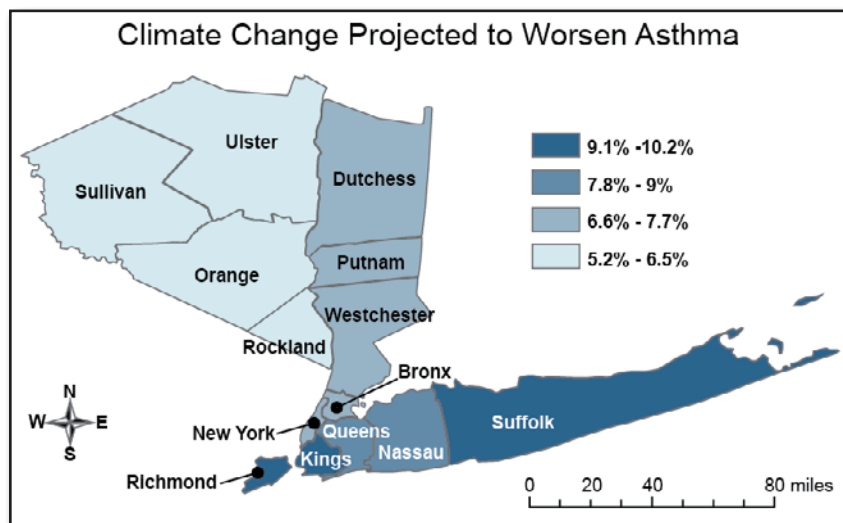
The interim assessment is further supported by a project of the President's Task Force on Environmental Health Risks and Safety Risks to Children. The task force, of which NIEHS is part, will convene this summer to discuss the particular impacts of climate change on children.

Global connections

The NCA focuses on the U.S., but makes clear that climate change is a global health problem. As a World Health Organization (WHO) Collaborating Centre for Environmental Health (see [story](#)), NIEHS is sharing the findings with counterparts in other countries.

Balbus noted that WHO discussed the issues of climate change and air pollution at its 67th session of the World Health Assembly in mid-May. "The NCA gave HHS Secretary Sebelius and Assistant Secretary Howard Koh, M.D., some important messages and information to bring to the world," said Balbus.

(Paula Whitacre is a contract writer with the NIEHS office in Bethesda, Maryland)



NCA, [Chapter 9](#), Figure 9.1: Projected increases in temperature, changes in wind patterns, and ecosystem changes will all affect future ground-level ozone concentrations. Climate projections using an increasing emissions scenario suggest that ozone concentrations in the New York metropolitan region will increase because of future climate change. This figure shows the estimated increase in ozone-related emergency room visits for children in New York in the 2020s (compared to the mid-1990s) resulting from climate change-related increases in ozone concentrations. Figure source: [Sheffield PE, Knowlton K, Carr JL, Kinney PL. 2011. Modeling of regional climate change effects on ground-level ozone and childhood asthma. Am J Prev Med 41\(3\):251-257.](#)

NCA key messages on human health

- 1. Climate change threatens human health and well-being in many ways**, including impacts from increased extreme weather events, wildfire, decreased air quality, threats to mental health, and illnesses transmitted by food, water, and disease-carriers, such as mosquitoes and ticks. Some of these health impacts are already underway in the U.S.
- 2. Climate change will, absent other changes, amplify some of the existing health threats the nation now faces.** Certain people and communities are especially vulnerable, including children, the elderly, the sick, the poor, and some communities of color.
- 3. Public health actions, especially preparedness and prevention, can do much to protect people from some of the impacts of climate change.** Early action provides the largest health benefits. As threats increase, our ability to adapt to future changes may be limited.
- 4. Responding to climate change provides opportunities to improve human health and well-being across many sectors**, including energy, agriculture, and transportation. Many of these strategies offer a variety of benefits, protecting people while combating climate change and providing other societal benefits.

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Centers of excellence program adds Texas consortium

By Eddy Ball

NIEHS has designated the Center for Translational Environmental Health Research (CTEHR) in Texas as the newest National Center of Excellence in Environmental Health Science. Led by veteran NIEHS grantee [Cheryl Walker, Ph.D.](#), CTEHR is a collaboration among [Texas A&M University \(TAMU\)](#), [Baylor College of Medicine](#), and the University of Houston, funded by a four-year, \$4.4 million NIH grant.

According to an [announcement](#) April 22 by the TAMU Health Science Center, CTEHR becomes the 21st [NIEHS Environmental Health Sciences \(EHS\) Core Center](#), serving as the cornerstone for integrated environmental health research, translation of research advances into practice, and community outreach and engagement aimed at improving human health.

The research base of the new center will focus on five thematic areas impacting human environmental health — early life exposures, chronic disease, metabolism, emerging technologies, and the microbiome, all the microorganisms that live in the human body.

“Understanding and mitigating environmental causes of diseases, such as asthma, heart disease, obesity, and cancer, offers the greatest opportunity to decrease disease burden,” said Walker, who also serves as director of the Texas A&M Health Science Center Institute of Biosciences and Technology. “Unlike genetic causes of disease, environmental exposures are modifiable, and if detected early, present opportunities for intervention to prevent disease occurrence and transmission to the next generation.”

Integrating existing resources into a team approach

The center represents a comprehensive team approach to addressing the more than one quarter of all deaths and disease, globally, that can be attributed to the environment. The top environmental health researchers, from each of the partners in CTEHR, bring expertise in a broad range of areas related to promoting human health. The research centers will also work with the Texas Medical Center in Houston, the largest medical center in the world with one of the highest densities of clinical facilities, anywhere, for patient care, basic science, and translational research.

In addition to exploring the connections between genetic traits and environmental health factors in humans, CTEHR researchers plan to call upon veterinary medical resources at TAMU, which houses the state’s only veterinary college, to advance the TAMU [One Health Grand Challenge](#). One Health refers to the link between animal, human, and environmental health. Animals and people share many diseases and are similarly affected by the environment.

A hallmark of the EHS Core Centers is their commitment to community engagement, which ensures that research findings can be translated into practical tools and resources for community residents, health care providers, public health practitioners, and policymakers. As part of these efforts, centers collaborate with



Walker came to TAMU three years ago from the University of Texas MD Anderson Cancer Center. She said the creation of CTEHR, as a hub for environmental health science research, was her priority from the beginning. (Photo courtesy of TAMU)

community partners to identify and address community concerns, increase public awareness of the potential health risks of exposures, and inform decision-making to reduce environment-related disease.

“We are delighted to welcome the CTEHR team into the Environmental Health Sciences Core Centers program fold. Under the leadership of Dr. Walker, and with its discovery pipeline and state-of-the-art resources, we expect the center will build teams to address complex questions in health, and of concern to communities, both locally and nationally,” said [Les Reinlib, Ph.D.](#), NIEHS EHS Core Centers program manager. “We are confident that the new center will enhance research and outreach on the interaction of genes with common exposures that may alter our risk for disease.”

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In addition to managing the EHS Core Centers grants, Reinlib is also the lead for the NIEHS [Breast Cancer and the Environment Research Program](#). (Photo courtesy of Steve McCaw)

Director of FNIH promotes foundation

By Kelly Lenox

During an April 21 visit to NIEHS, Maria Freire, Ph.D., president and executive director of the Foundation for the National Institutes of Health (FNIH), brought a welcome message of support to the researchers and leadership of NIEHS about this often-overlooked resource for NIH scientists.

NIEHS and NTP Director Linda Birnbaum, Ph.D., welcomed Freire warmly. “We are going to have a treat learning more about the foundation, which Dr. Freire calls ‘our foundation,’” Birnbaum said.

Freire explained that, although it is sometimes seen as a well-kept secret, [FNIH](#) can only achieve its goals if NIH researchers, including those beyond the Bethesda, Maryland campus, understand its role. “I hope to leave you with a sense of how the foundation can be helpful to you,” she told the attentive audience.

Independent and nimble

Freire first came to NIH in 1995, leaving in 2001 to become CEO of the Global Alliance for TB Drug Development, and later president of the Albert and Mary Lasker Foundation. “Through all of this time, I’ve never visited NIEHS,” she said. Appointed to her new role at the FNIH in November 2012, Freire was visibly pleased to be correcting that. “Our mission is to support the mission of NIH,” she said. “Without you, the foundation has no reason to be.”



Freire urged researchers to understand the perspective of funders. “Whether it’s \$10 or \$100,000, if I ask you for money, you’ll want to know what I’m going to do with it,” she said. “We have to justify every cent, so having realistic expectations and timelines is important.” (Photo courtesy of Steve McCaw)

As a nonprofit organization, FNIH is completely independent of NIH, though the directors of NIH and the U.S. Food and Drug Administration serve as ex officio members of the board of directors.

Freire described FNIH as a nimble organization, able to support a variety of goals and projects within NIH. Because it does not have an endowment, fundraising is the sole source for supporting projects, whether suggested by funders or proposed by researchers.

Adding NIEHS to the list

FNIH projects range from events and seminars to research projects, though research accounts for the vast majority of the funds allocated, according to Freire. Some projects originate with funders who approach FNIH with an interest in a particular research question or project. The foundation then searches out researchers interested in taking on the work.

Other projects originate with NIH researchers. The foundation then approaches funders likely to be interested in supporting it. NIH established an internal review process for such projects. Each institute or center (IC) conducts a scientific review of a project proposed by one of its scientists. Upon approval, the IC director sends the proposal to the NIH Office of the Director for review, which then forwards it to the Foundation. There is no application cycle, Freire explained. Funding requests are reviewed on a monthly basis by FNIH.

As she showed charts of how funds are allocated among projects and ICs, Freire noted that, at the moment, no NIEHS projects receive FNIH funding. “We need to change that,” she said.



Mary Wolfe, Ph.D., left, director of the NTP Office of Liaison, Policy, and Review, and Kent Stone, chief of operations in the NIEHS Office of the Scientific Director, both represent programs that could benefit from FNIH support. (Photo courtesy of Steve McCaw)



Among the attendees interested in correcting the current lack of FNIH funding for NIEHS and NTP research were, left to right, NIEHS Clinical Research Unit Medical Director Stavros Garantziotis, M.D.; Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training; and Tammy Collins, Ph.D., head of the NIEHS Office of Fellows' Career Development. (Photo courtesy of Steve McCaw)



Birnbau, right, led the question and answer session with Freire. (Photo courtesy of Steve McCaw)

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Pregnant and breastfeeding women need iodine supplements

By Robin Mackar

Women of childbearing years, especially those who are pregnant or breastfeeding, should take iodine supplements, according to new guidance by the American Academy of Pediatrics (AAP). “Many pregnant and breastfeeding women in the United States are not getting adequate supplies of iodine,” said Walter Rogan, M.D., head of the NIEHS Pediatric Epidemiology Group and lead author of the policy statement, which appears in the June issue of the journal *Pediatrics*. “Iodine produces thyroid hormone, which is critical for healthy brain development in children,” he said.

AAP recommendations

The new policy statement, “Iodine Deficiency, Pollutant Chemicals, and the Thyroid: New Information on an Old Problem,” offers recommendations for clinicians treating pregnant and breastfeeding mothers.

“Pregnant and breastfeeding women are particularly vulnerable to iodine deficiency. These women should make sure that they take a prenatal or lactation supplement that contains adequate amounts of iodine,” Rogan said. Pregnant and lactating women need about 290 micrograms of iodine a day. Iodized table salt can provide some of this, but most also need supplements containing at least 150 micrograms of iodine. Rogan pointed out that most processed foods are prepared with noniodized salt, so they do not help women meet the required iodine guidelines.

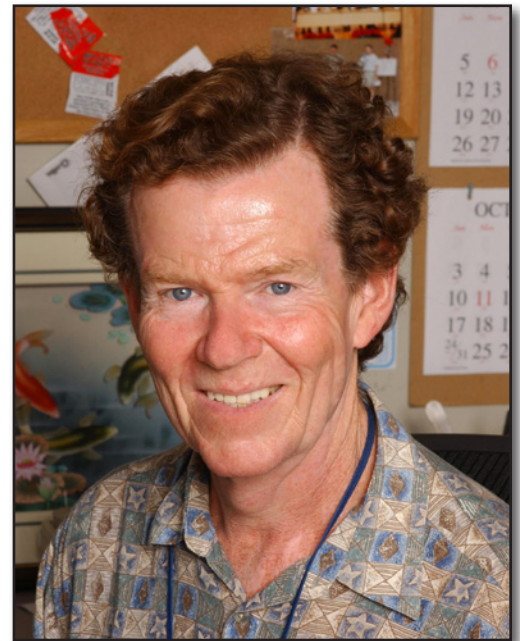
Although most pregnant and lactating women do take supplements, only about 15-20 percent take supplements containing iodine, according to the policy statement.

The statement also includes recommendations to federal, state, and local government agencies regarding iodine supplement labeling, and the need for safe drinking water and tobacco-free environments for children. Chemicals like nitrate, found in contaminated well water, and thiocyanate from cigarette smoke, can decrease iodine concentration. These chemicals are also difficult for infants to metabolize.

Iodine deficiency

Iodine deficiency can cause thyroid problems, which may affect a child’s cognitive development. Severe, untreated hypothyroidism in infancy can have serious, permanent effects on the brain.

Additionally, iodine deficiency in a mother can increase the vulnerability of both the mother and the child to the effects of certain environmental pollutants, including nitrate, thiocyanate, and perchlorate. Perchlorate is a chemical found naturally in arid climates and is used in the manufacture of solid rocket propellant for munitions, flares, and fireworks. It can contaminate drinking water and has been shown to disturb the normal production of thyroid hormones.



In 2012, Rogan was named an honorary fellow by AAP for his exemplary service with the group’s Council on Environmental Health (see [story](#)). (Photo courtesy of Steve McCaw)

Council on Environmental Health

The AAP [Council on Environmental Health](#), chaired by Jerome Paulson, M.D., of George Washington University, developed the policy statement. NIEHS Senior Advisor for Public Health John Balbus, M.D., now serves as the NIEHS liaison to the council, a role previously filled by Rogan.

The council advises the AAP board of directors, supports legislative initiatives, composes policy documents, and leads educational initiatives pertaining to environmental health and toxic exposures.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison, and a frequent contributor to the Environmental Factor.)

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Event helps employees laugh their way into ethical compliance

By Eddy Ball

NIEHS held its fifth annual Ethics Day May 15 with a refreshing mix of tunes, funny but instructional videos, good-natured competition, and serious talk about ethical conduct, with two keynote presentations and an informal brown bag discussion.

As she has in prior years, NIEHS and NTP Director Linda Birnbaum, Ph.D., joined members of the NIEHS [Ethics Office](#), headed by Bruce Androphy, J.D., for the event.

“It [Ethics Day] is really a very special way for us to come together and focus on some ethics issues and have some fun,” Birnbaum said in opening remarks. “We are the only institute at NIH [the National Institutes of Health] to have such an event, and it has been cited by Larry Tabak, [D.D.S., Ph.D.,] who is the principal deputy director for NIH and the NIH ethics officer, as a best practice.”

Birnbaum and Androphy opened the program with what has become an Ethics Day tradition — a song with original lyrics outlining ethical principles, sung to the tune of a classic from the world of country music, Johnny Cash’s “I Walk the Line.” The ditty ended with a serio-comic reference to filing of the annual financial disclosure document, Office of Government Ethics Form 278, by May 15 each year — “‘Cause I’m on time, I pay no fine.”

They continued another tradition with an Ethics Quiz Bowl, as the audience divided into teams competing for points by answering questions about government ethics.



With their spoof of the Johnny Cash ballad, “I Walk the Line,” Birnbaum, left, and Androphy set the tone for the fast-paced program that kept people laughing and learning for the next two hours. (Photo courtesy of Steve McCaw)

Rules of the road

As its first keynote speaker, the program welcomed Justina Fugh, J.D., senior counsel for ethics at the U.S. Environmental Protection Agency (EPA). Fugh built her presentation around “Ethical Rules of the Road,” using a traffic metaphor to discuss rules related to official and personal capacity in outside activities.

Fugh seasoned her talk with humor, with jokes about her family life, fellow employees at EPA, and government employment. But, her message was an important one — “Stay in your own lane, signal your intentions clearly, and consult with your ethics officials.”

When employees want to engage in outside activities, they need to make sure they obtain prior ethics approval. When they engage in activities in a personal capacity, they need to avoid even the slightest appearance of using their official affiliations with a government agency as a calling card.

As Fugh told the audience, “When you became a government employee, you gave up some of your civil rights.” She cautioned employees that it is their responsibility to make sure they understand what those rights are.

An exciting time for people concerned about biomedical ethics

The focus and tone of the program changed dramatically with a telecast presentation on “NIH Ethics and Policy Priorities,” by [Kathy Hudson, Ph.D.](#), deputy director for science, outreach, and policy at NIH. Hudson set her sights on big picture issues with national implications.

Hudson described the NIH response to ongoing ethical controversies over the protection of human subjects in the famous HeLa cell line case, and the standard of care in clinical trials. She described the process NIH is now leading to substantially revise ethical guidelines, to ensure that participants in biomedical research will have even greater rights to information about risk, and stronger protection of their individual privacy.

Hudson outlined important documents and principles developed over the last half of the 20th century, as well as ongoing efforts by NIH to reform the Common Rule for the Protection of Human Subjects in Research, to meet the unprecedented ethical challenges posed by new developments and technological advances in biomedical research in the 21st century, such as modern genomic technology.

After a short break, many attendees regrouped for a discussion over lunch led by Meave Tooher, J.D., on “Defending Government Employees Investigated or Charged With Ethical Misconduct.” Tooher is a partner in an Albany, New York-based law firm, with expertise in representing individuals in cases involving ethics, government compliance, and administrative and municipal law.



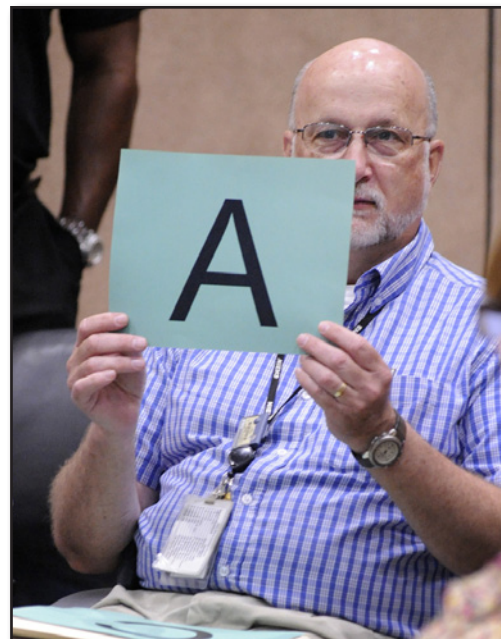
Fugh’s routine was a standup mix of self-deprecating humor and straight talk about the responsibilities of federal employees engaged in outside activities, such as serving on boards and other entities. “If you’re confused, you should ask your ethics office first,” she said. (Photo courtesy of Steve McCaw)



Like biologist Justin Kosak, right, and Joan Packenham, Ph.D., director of the NIEHS Office of Human Research Compliance, most of the audience spent most of the program laughing along with organizers. (Photo courtesy of Steve McCaw)



NIEHS Ethics Office members Patricia Harris, left, and D.J. Joya emceed the Ethics Quiz Bowl, which had its share of silly items among the multiple-choice questions. Ethics staff also produced tongue-in-cheek video cartoons communicating some important ethics information. (Photo courtesy of Steve McCaw)



Radiation Safety Officer Bill Fitzgerald, was part of one of the four teams competing for points in the Ethics Quiz Bowl. (Photo courtesy of Steve McCaw)



Hudson's presentation had a sobering effect on the audience, as evidenced in the thoughtful expression on the faces of NIEHS Scientific Director Darryl Zeldin, M.D., right, and NIEHS Clinical Research Unit Medical Director Stavros Garantziotis, M.D. (Photo courtesy of Steve McCaw)



Hudson's talk also explored efforts to encourage greater sharing of clinical trial results and enhance data sharing. "We want to get all of our data into the public domain," she said. (Photo courtesy of NIH)



Toohar, left, has been a regular at NIEHS Ethics Days, serving as a keynote speaker and discussant. Now in private practice, she is an attorney who formerly worked with Androphy at the New York State Commission on Public Integrity. (Photo courtesy of Steve McCaw)

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Variety of topics covered at council

By Ernie Hood

At its 142nd [meeting](#) May 13-14, the National Advisory Environmental Health Sciences Council covered a wide variety of topics. The group learned about various NIEHS activities, provided feedback on programs, and gave thoughtful consideration to current issues in environmental health research.

Budget uncertainty

NIEHS and NTP Director Linda Birnbaum, Ph.D., reported that the fiscal year 2015 budget outlook is essentially flat. Despite the budget deal reached in Congress in December 2013, a finalized budget is unlikely in the near future, due to ongoing contention about the Affordable Care Act.

“We expect that there will be a series of continuing resolutions,” she predicted. Birnbaum expressed hope that there would be only one continuing resolution in late September, which would carry through the November mid-term election.

On a brighter note, Birnbaum announced that a candidate has been identified to fill the NIEHS Clinical Director opening, with the expectation that the hiring will be finalized by late summer or early fall. “We’re very excited,” she said. “I think this is going to take our clinical program to the next level.”

Grantee opportunities

Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, discussed the new National Institutes of Health (NIH) process for resubmission of grant applications following two prior rejections. “It’s probably the biggest thing that’s happened in the extramural [grantee] community in the last couple of years,” she noted.

Collman also described a new NIH Early Career Reviewer Program designed to train qualified early-career scientists to become effective Center for Scientific Review (CSR) grant reviewers. “It’s a nice opportunity to make your way through NIH, to meet people at CSR, and make the contacts necessary for success in the future,” she said.



In addition to her usual updates on NIEHS and NTP personnel changes, science advances, news and highlights, and awards and recognitions, Birnbaum briefed council members on the establishment of two newly formed groups — an exposome faculty and an inflammation faculty — who are working to guide implementation of NIEHS strategic plan goals. (Photo courtesy of Steve McCaw)



Collman described an initiative to reassign grants among program administrators, following the recent division reorganization. “We’ve made some moves in terms of balancing the workload, and also infusing some new ideas and perspectives into some of the areas,” she said. (Photo courtesy of Steve McCaw)

Project update

Senior Medical Advisor Aubrey Miller, M.D., briefed the council on developments related to the [NIH Disaster Research Response Project](#). One of the major elements of the project is a central repository of data collection tools and research protocols.

The [website](#) currently provides 60 tools, with another 200 selected for eventual inclusion. The tools will allow timely collection of important baseline data in disaster situations.

Miller announced formation of a new Environmental Health Science Disaster Research Network that includes NIEHS researchers and grantees, NIEHS-sponsored research centers, the Worker Education and Training Program, and community partners. The goal is to build a national network for rapid response to future environmental threats and disasters, with immediate inclusion of environmental health research questions.

Biomedical research paper discussion

The council also engaged in a dialogue about a thought-provoking paper by Alberts et al., “[Rescuing US biomedical research from its systemic flaws](#),” recently published in the Proceedings of the National Academy of Sciences.

Of the many suggestions in the paper, council discussion centered largely on the authors’ recommendations that the number of NIH trainees should be decreased and the number of staff scientists should be increased, and that individuals, rather than projects, should be funded.

Council members disagreed with a number of the points made by the authors, although the postdocs in the room strongly supported the idea of increasing postdoctoral stipends and making changes to free up additional positions for advancement.

Thumbs up

Council approved a concept for the next phase of the Breast Cancer and the Environment Research [Program](#), consisting of a Transdisciplinary Research Initiative and a Communication Research Initiative, with \$38 million in funding costs, over five years, shared between NIEHS and the National Cancer Institute.

Crosstalk: the innate immune system and cholesterol trafficking

Following the tradition of asking recently tenured Division of Intramural Research scientists to brief the council on their work, Michael Fessler, M.D., addressed the panel about his group’s groundbreaking [research](#) on regulation of the innate immune response to the environment by cholesterol trafficking.

Fessler, lead of the NIEHS [Clinical Investigation of Host Defense Group](#) within the Laboratory of Respiratory Biology discussed “A Bench-to-bedside Study of *APOE4* in the Human Innate Immune Response.”

His group hypothesized that cholesterol trafficking and innate immunity signaling are intrinsically coupled processes, and that perturbation in one will regulate the other. He showed data indicating that the E4 allele of the *APOE* gene, which encodes the key lipid-trafficking and immunomodulatory protein called apolipoprotein E, is a fundamental determinant of the human innate immune response. The investigation included studies conducted in the NIEHS [Clinical Research Unit](#).

Subjects with two copies of the *APOE4* gene appear to be at heightened risk for a broad array of inflammatory diseases, including infectious and noninfectious environmentally-induced disorders, in which the innate immune response has been implicated. “We would submit that *APOE4* positivity should now be studied for potential impact on illness severity in a wide range of inflammatory diseases,” Fessler said.

People with an *APOE3/APOE4* genotype — about 20 percent of the U.S. population — also have been shown to exhibit heightened innate immune responses, compared to individuals with the more common *APOE3/APOE3* genotype.

Fessler speculated that the findings could lead to customization or tailoring prognoses and treatments, based on genetic and environmental risk factors.

The panel also approved a new evaluation of the Environmental Health Sciences Core [Centers](#) Program to be conducted over the next year.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



Among the new council members attending their first meeting were Marie Lynn Miranda, Ph.D., left, from the University of Michigan, and Kevin Elliott, Ph.D., from Michigan State University. (Photo courtesy of Steve McCaw)



Fessler gave the traditional council science talk (see [text box](#)). In his introduction of Fessler, NIEHS Scientific Director Darryl Zeldin, M.D., said, “He is a triple threat — an active clinician, as well as a basic scientist and a clinical teacher.” (Photo courtesy of Steve McCaw)



Vivian Cheung, M.D., right, of the University of Pennsylvania, listens during the discussion of the biomedical research paper, as Edward Postlethwait, Ph.D., from the University of Alabama at Birmingham, said that more information was needed about the job market for trainees. “What’s the number of potential job opportunities out there for Ph.D.-trained scientists that are not in academia?” he asked. (Photo courtesy of Steve McCaw)



Monica Frazier, Ph.D., Intramural Research Training Award fellow in the Mechanisms of Mutation Group and chair of the NIEHS Trainees’ Assembly, said that over her two years as a postdoc at NIEHS, she had seen very few of her postdoctoral colleagues go on to jobs in academia. “As we’re looking at the job market, the people who have the jobs we want to have are twice our age,” she noted. “How do we move into this when our mentors, who are the experts, are never retiring? There’s no job to be had, so we pursue alternative paths.” (Photo courtesy of Steve McCaw)



Council member Linda McCauley, Ph.D., R.N., from Emory University, was pleased with what she heard at the meeting. (Photo courtesy of Steve McCaw)



Council member Viola Waghiyi, right, Environmental Health and Justice Program director at the Alaska Community Action on Toxics, said attention should be paid to food security issues as part of disaster preparedness. She related how, at her home on St. Lawrence Island in the Bering Sea, climate change has already severely affected the availability of traditional foods upon which the native population relies. (Photo courtesy of Steve McCaw)

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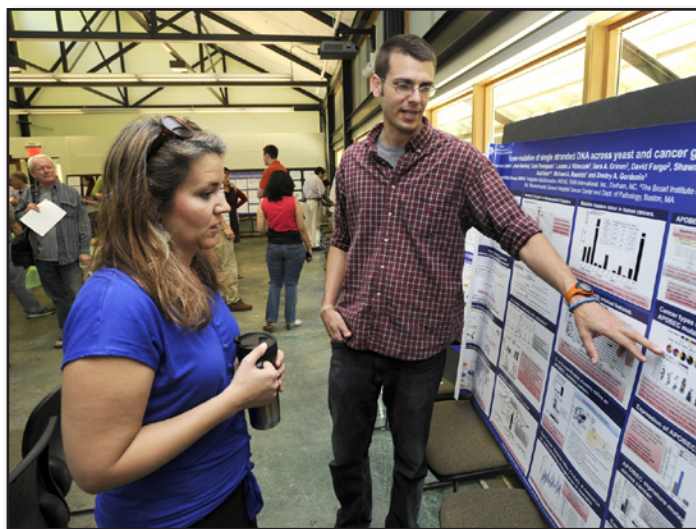
Molecular genetics groups break for annual retreat

By Deepa Singh

The NIEHS Laboratory of Molecular Genetics (LMG) kicked off its two-day departmental retreat May 8 at the North Carolina Botanical Garden on the campus of the University of North Carolina at Chapel Hill (UNC). The event, organized by the LMG Trainee Action Committee (TAC), included scientific talks by academic investigators and career talks by former LMG trainees now working in a range of scientific careers.

Attended by more than 60 lead researchers and trainees from LMG, the retreat had a mixed feeling of career fair and scientific conference. The event was meant to provide current trainees with a chance to interact and seek career advice from a wide range of speakers (see [textbox](#)).

According to Bill Copeland, Ph.D., head of LMG, the retreat was organized to help trainees as they face a changing job market. “Along with the excellent scientific presentations, we wanted a program that included professionals who had opted for traditional postdoc career routes, such as academia and industry, as well as those who had chosen nonbench careers, such as regulatory affairs, science writing, grant review, and management,” he said. “As senior scientists, we realize we can no longer assume that trainees will necessarily follow the same path we did decades ago.”



During a morning break, Steven Roberts, Ph.D., right, who is an Intramural Research Training Award fellow in the Chromosome Stability Group headed by Mike Resnick, Ph.D., explained his research work to Tammy Collins, Ph.D., director of NIEHS Office of Fellows' Career Development. (Photo courtesy of Steve McCaw)

Academic speakers discuss recent advances

Academic speakers at the retreat are long-standing experts in their fields, who provided insights into recent advances in leading-edge technologies, such as electron microscopy and next-generation sequencing.

- Jack Griffith, Ph.D., of the UNC Lineberger Comprehensive Cancer Center presented his exciting work on providing visual representations of the loading of DNA replication proteins onto the DNA in bacteriophage T7 and T4, and herpes simplex virus-1. These studies were conducted using transmission electron microscopy and, according to Griffith, together with X-ray crystallography, this technique will provide some of the structural answers that will be critical for examining the similarities and differences across various systems.
- Piotr Mieczkowski, Ph.D., director of the next-generation sequencing and genotyping facility and a professor with the Lineberger Comprehensive Cancer Center at UNC, talked about how next-generation sequencing allows a cheaper, relatively faster and more extensive way of diagnosing inherited diseases.
- Susan Lovett, Ph.D., professor of biology at Brandeis University, described a distinct class of mutagens, widely used in the treatment and prevention of HIV/AIDS, that promote DNA template switching, thereby leading to stalling of the replication fork.
- Duke University cancer biologist David MacAlpine, Ph.D., explored the effects of chromatin architecture in defining the eukaryotic start sites of DNA replication.

Former LMG trainees help guide current trainees

The retreat also gave LMG postdocs a chance to network with a panel of former trainees who have sought careers in other than tenure-track positions. The former trainees talked about how they prepared for the jobs they hold, their responsibilities and experiences at their current jobs, and the various career development opportunities they took advantage of while at NIEHS. They also emphasized the importance of networking and developing management and leadership skills in the different workshops they attended at NIEHS.

Career panelists explore life away from the tenure track

- Christopher Halweg, Ph.D., lecturer of biological sciences at N.C. State University
- Shannon Holmes, Ph.D., senior manager of regulatory affairs at Biogen Idec
- Andres Larrea, Ph.D., application sales representative at Pacific Biosciences
- Robert Kokoska, Ph.D., program manager at the U.S. Army Research Office
- Omari Bandele, Ph.D., toxicology reviewer at the U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition
- Rajesh Kasiviswanathan, Ph.D., purification development scientist at FUJIFILM Diosynth Biotechnologies
- Rich Gradman, Ph.D., managing editor at American Journal Experts



Career talks by former LMG members were the highlight of the first day. Larrea, left, and Holmes, former members of the NIEHS DNA Replication Fidelity Group, led by Thomas Kunkel, Ph.D., shared their experiences at their current jobs. (Photo courtesy of Steve McCaw)

The retreat included a poster flash session, with presenters talking briefly about their research subject, using only one slide. The exercise encouraged the scientists to be creative about their projects and served as a kind of thumbnail advertisement of their work.

(Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group.)



MacAlpine, center, an associate professor at Duke University and one of the scientific speakers, listened to the other talks and contributed to the career panel discussions. (Photo courtesy of Steve McCaw)



From right, Katarzyna Bebenek, Ph.D.; Carl Anderson, Ph.D.; and Thomas Kunkel, Ph.D., pondered the advice former LMG trainees shared with others. (Photo courtesy of Steve McCaw)



LMG members came together for a group photo early in the departmental retreat. Seated in the front row, from left, are lead researchers Marilyn Diaz, Ph.D.; Douglas Bell, Ph.D.; Jan Drake, Ph.D., former chief of LMG; Copeland; Resnick; Roel Schaaper, Ph.D.; and Kunkel, who holds a dual appointment in the NIEHS Laboratory of Structural Biology. (Photo courtesy of Steve McCaw)

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Genomics Day highlights breadth of NIEHS resources and research

By Staton Wade

NIEHS and EPA scientists gathered May 1 for the fifth annual Genomics Day. The event increases awareness of the vast array of genomics resources available to NIEHS researchers and promotes discussion about the research those resources support throughout the Institute.

Kevin Gerrish, Ph.D., deputy director of the NIEHS Molecular Genomics Core, organized and moderated the event. Highlights included a keynote address, talks from junior researchers and trainees (see text box), and a poster session, featuring 29 posters on genomics research by NIEHS and EPA scientists, and 18 posters on genomics services and products available from support groups.

Core facilities provide new genomics technologies

During his opening remarks, Gerrish highlighted new technologies available to researchers through the Molecular Genomics Core, including the NanoString nCounter Analysis System, and new high content arrays for gene expression and DNA methylation analysis.

Greg Solomon, manager of the NIEHS Epigenomics Core, explained that he and his staff have been busy providing next generation sequencing data to NIEHS researchers and maximizing the output of their Illumina MiSeq sequencers. The Epigenomics Core has performed almost 500 runs since this technology became available. “These instruments run basically nonstop in my laboratory,” said Solomon.

To analyze the wealth of data generated by the core facilities, David Fargo, Ph.D., head of the Integrative Bioinformatics Group, pointed out that his team supports investigators at multiple levels, from simple analyses to the development of custom bioinformatics tools. “The real goal is to be scientific collaborators, and this involves integration of data for meaningful biological discovery,” he explained.

The power of genomics for disease prediction

Steven Kleeberger, Ph.D., head of the NIEHS [Environmental Genetics Group](#) in the Laboratory of Respiratory Biology, gave the keynote address.

Genomics Day talks by NIEHS fellows and junior researchers

- **Mallikarjuna Metukuri, Ph.D.**, research fellow in the [Metabolism, Genes, and Environment Group](#), used microarray gene expression analysis to demonstrate how the metabolic regulator SIRT1 affects intestinal homeostasis, inflammation, and the gut microbiome.
- **Diana Cruz-Topete, Ph.D.**, research fellow in the [Molecular Endocrinology Group](#), used microarray technology to define a novel role for the glucocorticoid receptor in the electrophysiology of the heart.
- **Daniel Menendez, Ph.D.**, staff scientist in the [Chromosome Stability Group](#), combined microarray analysis and next generation sequencing to identify novel targets of the p53 tumor suppressor involved in innate, or nonspecific, immunity.
- **Li Wang, Ph.D.**, visiting fellow in the [Stem Cell Biology Group](#), used the results of a genomic screen to identify the THO complex as a RNA exporter required for self-renewal of embryonic stem cells.
- **Mehmet Karaca, Ph.D.**, postdoctoral fellow in the [Environmental Genomics Group](#), performed genome-wide expression analysis of both messenger RNA and microRNA to explore the role of transcription factor NRF2 in adipogenesis, or the cell differentiation process leading to adipocytes, or fat cells.
- **Sophia Harlid, Ph.D.**, postdoctoral fellow in the [Molecular and Genetic Epidemiology Group](#), used DNA methylation arrays to study the epigenetic effects of phytoestrogen exposure in infants who are fed soy formula.

Kleeberger described how his lab uses both genomic and transcriptomic data to identify gene signatures that predict susceptibility to respiratory syncytial virus (RSV).

RSV causes 160,000 deaths, worldwide, and the hospitalization of 144,000 children in the U.S. every year, explained Kleeberger. By identifying genes associated with RSV susceptibility, he hopes to be able to predict disease severity, prior to infection, and identify patients who would most benefit from preventative measures.

(Staton Wade, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Chromatin and Gene Expression Group.)



Gerrish noted that Genomics Day promotes awareness of available resources, as well as enhances collaboration with local EPA colleagues. (Photo courtesy of Steve McCaw)



Keynote speaker Kleeberger led a research team that used genome-wide association mapping to identify a gene that may make premature infants susceptible to a chronic lung disease called bronchopulmonary dysplasia ([summary](#)). (Photo courtesy of Steve McCaw)



Solomon described the techniques used in the newest core at NIEHS — the Epigenomics Core — which has made powerful next generation sequencing technology available on-site to researchers. (Photo courtesy of Steve McCaw)



In addition to the bioinformatics services his group provides, Fargo described the computing resources available to researchers at NIEHS, which include a new parallel processor, servers that host hundreds of software applications, and nearly a petabyte of storage optimized for big data science. (Photo courtesy of Steve McCaw)



After his talk on oxidative stress and adipogenesis, Karaca, center, took advantage of the poster session to discuss the bioinformatics tools available to NIEHS scientists. (Photo courtesy of Steve McCaw)



Biologist Yin Li, Ph.D., of the NIEHS Receptor Biology Group, was excited to discuss her work with visiting fellow Motoki Takaku, Ph.D., of the Eukaryotic Transcriptional Regulation Group. Li presented a poster on the role of the estrogen receptor in mediating the epigenetic effects of diethylstilbestrol (DES) exposure in reproductive organs. (Photo courtesy of Steve McCaw)

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NIEHS Biomedical Career Symposium draws hundreds

By Monica Frazier

The 17th annual NIEHS Biomedical Career Symposium opened April 25 with a warm welcome from NIEHS Scientific Director Darryl Zeldin, M.D. An estimated 350 attendees, eager for professional advice on next steps in their careers, filled the meeting rooms at the U.S. Environmental Protection Agency (EPA) campus in Research Triangle Park, North Carolina.

Zeldin challenged participants to design and commit to a plan for transition to a rewarding career in the biomedical sciences. “For many of you, the decisions you make over the next year or two will shape your lives as scientists for decades to come,” Zeldin said. “Better understanding of the various options available to you, and what it takes to pursue specific career paths, is absolutely essential for making those important decisions.”

Transitions through networking

[Kristin Gabor, Ph.D.](#), co-chair of the event, reiterated Zeldin’s remarks, noting that this year’s symposium focused on successful transitions into a variety of career paths. One foundation for a career transition is the development of a professional network, which is why the committee invited [Alaina Levine](#), president of Quantum Success Solutions and author of the upcoming book “Networking for Nerds,” to deliver the keynote address.



Levine, who led highly-rated workshops at last year’s symposium, informed and entertained attendees as she discussed the critical need for scientists to develop a professional network. (Photo courtesy of Steve McCaw)

Levine's talk, "Accessing Hidden Career Opportunities Through Networking and Reputation Management" set the tone for the day. Using a medley of stories from her own experiences — and her signature comedic style — Levine entertained the audience, while educating them on the value of networking and self-branding.

"Upwards of 90 percent of jobs are gotten through hidden opportunities, which are made available to you from networking," Levine said. She told how admiring the shoes of the woman next to her on a flight led to paying work — the shoes were on the feet of a congressman's wife who needed help using humor in her speeches.

"You need diverse influences and diverse sources of inspiration — people who can give you new ideas and help you solve the problems you are trying to solve in your scientific discipline," Levine added. "This diversity of sources comes from networking."

Something for everyone

The day was packed with sessions, including 10 expert panels from various career paths, 10 career development workshops, and a networking reception featuring exhibitors from local groups and companies.

"We sought out speakers on a range of topics to support career transitions, from how to network and how to interview, to what steps to take to land that job," said Gabor. "While we wanted our workshops to meet varied interests, the primary goal was to showcase the plethora of opportunities available to those with a biomedical degree," she added.

Organizers also arranged for 25 professionals to review CVs and resumes of more than 175 participants. The reviewers were categorized so attendees could choose the most appropriate expert in their desired career path, whether industry, government, or academia.

Postdoc-led event

The annual event, which is planned, organized, and carried out by NIEHS and EPA postdoctoral fellows, was an impressive display of teamwork and dedication to educating the scientific community about career opportunities and advancement strategies.

Co-chairs Gabor and [Bethany Hsia, Ph.D.](#), led a 25-member committee (see [text box](#)), which began work last fall. Committee members selected and invited panelists, organized arts and photography, managed facility resources, and led social media advertisement, earning transferable skills and developing contacts that will help them in their own career development.

The committee's collaboration and effort was praised by [Tammy Collins, Ph.D.](#), director of the NIEHS Office of Fellows' Career Development. Collins assisted in behind-the-scenes planning and logistics, and the co-chairs noted that Collins' experience and advice were invaluable.



Zeldin applauded the efforts of the 2014 career symposium planning committee. (Photo courtesy of Steve McCaw)



John Vandenberg, Ph.D., Director of the EPA National Center for Environmental Assessment and Director for the Human Health Risk Assessment Program, welcomed participants to the EPA campus, noting the outstanding participation and excitement at the event. (Photo courtesy of Steve McCaw)



During the coffee break, Alexandria Marchi, Ph.D., right, and another attendee look through the symposium booklet, a shortened version of the lengthy program from previous years. One of the committee's priorities was to reduce the carbon footprint of the symposium. (Photo courtesy of Steve McCaw)



Lori Conlan, Ph.D., of the NIH Office of Intramural Training and Education, advised participants in her conflict management workshop on techniques for approaching difficult conversations. She then provided a chance to practice giving and receiving personal feedback. (Photo courtesy of Steve McCaw)



Melanie Jardim, Ph.D., right, of United Therapeutics, and Jeffrey Stumpf, Ph.D., former NIEHS postdoctoral fellow and now a writer at MedThink, took questions from the crowd during the Science Communication and Writing career panel. (Photo courtesy of Steve McCaw)



The planning committee relocated the coffee and snacks, funded by donations from NIEHS and EPA postdocs and staff, to the EPA Atrium this year, allowing a constant flurry of discussion between attendees and with exhibitors, both during breaks and the afternoon networking reception. (Photo courtesy of Steve McCaw)



According to Gabor and Hsia, the large number of volunteers on the career symposium planning committee, from NIEHS and EPA, allowed them to dedicate two members to outreach and social media advertising for the symposium. This was a major success, with symposium attendance up by more than 100 over last year. (Photo courtesy of Steve McCaw)

17th Annual NIEHS Career Symposium Planning Committee

Kristin Gabor, Ph.D. — Co-chair

Kelly Daughtry, Ph.D.

Emmi Felker-Quinn, Ph.D.

George Fromm, Ph.D.

Eugene Gibbs-Flournoy, Ph.D.

Juhee Haam, Ph.D.

Melissa Hausburg, Ph.D.

Julie Lowe, Ph.D.

Marie McGee, Ph.D.

Clinton Orebaugh, Ph.D.

Samantha Snow, Ph.D.

Katoria Tatum-Gibbs, Ph.D.

Staton Wade Ph.D.

Lauren Wilson, Ph.D.

Bethany Hsia, Ph.D. — Co-chair

Shannon Farris, Ph.D.

Monica Frazier, Ph.D.

Samuel Gattis, Ph.D.

Kymberly Gowdy, Ph.D.

Sophia Harlid, Ph.D.

Kristin Lichti-Kaiser, Ph.D.

Shaun McCullough, Ph.D.

Jennifer Nichols, Ph.D.

Simone Otto, Ph.D.

Natacha Steinckwich-Besancon, Ph.D.

Kirsten Verhein, Ph.D.

Jeremy Weaver, Ph.D.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Mechanisms of Mutation Group.)

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Emerging concerns with PCBs in schools draw hundreds to SRP webinars

By Sara Mishimandani

An international group of more than 300 people gathered, via webinar, April 21 and April 28, to discuss the issues related to the presence of polychlorinated biphenyls (PCBs) in schools. The webinars were part of the NIEHS Superfund Research Program (SRP) [Risk e Learning seminar series](#). In the last ten years, PCBs have been detected in many school buildings built before the late 1970s, due, in part, to fluorescent light ballasts and interior and exterior caulk containing PCBs.

“The webinar series was the result of a multiagency working group, coordinated by SRP, that identified PCBs in schools as a potential problem that may have implications for many school systems nationwide,” said Heather Henry, Ph.D., SRP program administrator. “The webinar was an opportunity to bring more attention to this issue.”

NIEHS and U.S. Environmental Protection Agency (EPA) staff, SRP grantees, and international partners explained the issues and presented approaches to reducing environmental PCB exposure in schools. Each two-hour session allowed researchers, risk assessors, members of state and local governments, and members of federal agencies from around the country and around the world to discuss exposure assessment and PCB-associated health risks.



Henry introduced the speakers and moderated the second session, which focused on identifying and reducing health risks from PCBs in schools. (Photo courtesy of Steve McCaw)

Overview and exposure assessment

PCBs are semivolatile chemicals, manufactured in the U.S., and used widely in products such as paints and cements, fluorescent light ballasts, sealants, and adhesives. According to Mark Maddaloni, Ph.D., EPA regional risk assessment coordinator, although PCBs were banned from use in the U.S. more than 30 years ago, they still exist in old products and buildings built before 1979. They also linger in groundwater and soil.

[Kent Thomas, Ph.D.](#), a research physical scientist in the EPA National Exposure Research Laboratory, detailed EPA findings on the sources and levels of PCBs in indoor environments — schools in particular. He described the current knowledge and uncertainties that need to be overcome to allow for better mitigation, or reduction, of these contaminants. Thomas also provided information and EPA resources on testing for PCBs, renovating and removing PCB-containing caulk, and additional resources for parents and teachers.

[Peter Thorne, Ph.D.](#), director of the NIEHS-funded Environmental Health Sciences Research Center at the University of Iowa, discussed human exposure to PCBs, including routes of exposure and approaches to reducing exposures. Using examples from the University of Iowa Airborne Exposures to Semivolatile Organic Pollutants study, funded jointly by SRP and an NIEHS Environmental Health Sciences Core Center grant, Thorne discussed development of a model to better understand PCB exposure in various environments.

Identifying and reducing health risks

During the second session, University of Iowa researcher [Gabriele Ludewig, Ph.D.](#), provided an overview of the mechanisms of PCB toxicity, addressing airborne PCB exposures at levels found in school environments.

EPA toxicologist Geniece Lehmann, Ph.D., discussed evaluating the health risks of PCBs in indoor air and described critical areas of research needed to better evaluate risks for inhaled PCBs. According to [EPA](#), PCB exposure has been associated with a reduction in IQ, increased risk of attention deficit disorder, and hormonal and immune disruptions, among other health problems. PCBs are also known to cause cancer in animals and are considered possible carcinogens in humans.

The final presenter, Niklas Johansson, Ph.D., of the Swedish Environmental Protection Agency, shared an international experience on reducing PCB exposure risks. Sweden enacted legislation addressing nationwide identification, removal, and destruction of PCBs used in open applications, such as buildings and construction sites. Johansson discussed the successful identification and removal of PCBs in buildings and construction sites in Sweden, and how it can be done elsewhere.

Archives of both the [April 21](#) and [April 28](#) presentations, including supporting slides, can be found on the EPA Clean-up Information website.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

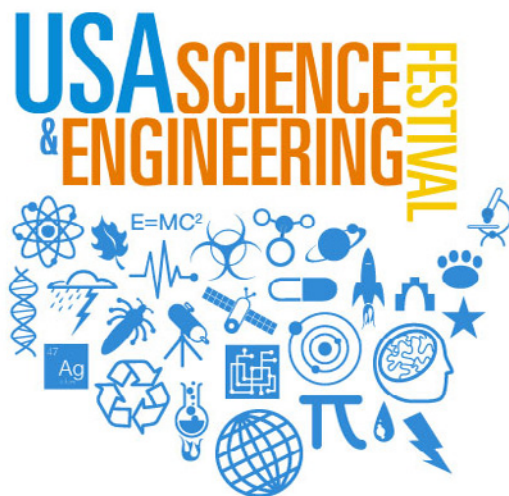
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NIEHS reaches out at nation's largest STEM event


By Eddy Ball

Members of the NIEHS Office of Science Education and Diversity (OSD) were part of a trans-NIH effort April 26-27 at the 2014 [USA Science and Engineering Festival](#) in Washington, D.C., as well as pre-event activities April 25.

More than 750 leading science, technology, engineering, and mathematics (STEM) organizations gathered at the two-day expo, held at the Walter E. Washington Convention Center. The event, attended by an estimated 350,000, marked the culmination of school programs, contests, and events held nationwide during 2013.





NIH was an official partner of the 2014 USA Science and Engineering Festival, joining a number of private and public sector entities lending their support to make the event a rousing success.



Linked video:
[For a sample of the excitement of the festival, watch the highlight video from the second festival, held in 2012 \(04:59\)](#)

LARRY BOCK
USAEF FOUNDER

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Along with helping to staff the NIH Pavilion, [OSD](#) Director Ericka Reid, Ph.D., and K-12 Science Education and Outreach Coordinator Huei-Chen Lao, with some additional help from Mary Gant of the NIEHS Bethesda Office, gave a demonstration of the popular respiratory health exercise. The exercise was developed by NIEHS postdoc volunteers, for use at their Citizen Schools outreach programs at Lowes Grove Middle School in Durham, North Carolina (see [story](#)).

Visitors to the exhibit tested their lung capacity, using a regular-sized straw to simulate a normal airway, and a cocktail straw to simulate a restricted airway that asthma patients suffer, exhaling fully into an inverted 5-liter water-filled bottle set inside a bucket filled with water. The amount of water displaced by the air indicated the participant's lung capacity.

The festival was free and offered attendees the additional opportunity to win an iPad 2, video games, science books, tee shirts, and other prizes, as well as a chance to meet They Might Be Giants and Bill Nye the Science Guy.

"It was an incredible experience," Reid said afterwards, "packed full of interesting science and engineering activities for people of all ages." The festival featured more than 3,000 hands-on STEM activities and some 150 stage shows.

NIH on the front lines of STEM promotion

The One NIH effort was coordinated through the NIH Office of the Director by Jennifer Gorman Wright, communications director for the Division of Program Coordination, Planning, and Strategic Initiatives. In addition to NIEHS, more than 20 NIH institutes and centers participated in the ten meetings to plan activities, NIH Pavilion layout and exhibitor logistics, and coordination of NIH volunteers.

Hundreds of NIH scientists and staff committed time and effort to provide challenging and interactive exhibits. NIH also hosted career exploration information sessions in the Career Pavilion, where attendees could meet with NIH scientists, health communicators, and other health professionals, to find out why they love science and have committed to science as their career choice.



Shown at the outreach program in May 2013 (see [story](#)), Lao, left, and Reid carried good ideas from the field to this year's USA Science and Engineering Festival. (Photo courtesy of Steve McCaw)



NIEHS biologist Mercedes Arana, Ph.D., left, led students through the prototype lung capacity exercise in 2012 at Lowes Grove Middle School. Reid and Lao demonstrated the popular exercise at the festival. (Photo courtesy of Steve McCaw)



As visitors at the NIEHS demonstration in Washington also learned, the proof (for lung capacity) was in the bucket. (Photo courtesy of Ericka Reid)

In addition to the NIEHS lung capacity measurement exercise at the Health and Medicine Pavilion, attendees could also find out how NIH researchers are advancing science using new 3-D printers that transform digital files into physical objects, see the brain in action, and learn how to become a forensic detective.

Along with broad participation by NIH, the festival has enjoyed enthusiastic support from other federal agencies and the White House. President Barack Obama welcomed participants to the 2012 festival, and White House Office of Science and Technology Policy Director John Holdren, Ph.D., kicked off this year's event.

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Translating research into products to improve public health

By Sara Mishamandani

What do a new eco-friendly cleanup chemical, a mercury-sensing device, and pathogen-detection technology have in common? They are all products of small business startups spun out of NIEHS-funded basic research, recognized for innovation. The products, from scientists at the University of Arizona (UA); University of California (UC) Berkeley; and UC Davis, promise to enhance public health by providing lower-cost and safer approaches to cleaning and detection of contaminants.

Development of natural eco-friendly surfactants

Raina Maier, Ph.D., director of the UA Superfund Research Program (SRP), and her colleagues were recently honored with a UA Catapult Award, for their work developing microbially produced surfactants, or biosurfactants, which they are patenting and commercializing through a startup chemical company, [GlycoSurf](#). The Catapult Award recognizes the application of innovative UA research to improve the lives of people in Arizona and around the world.

GlycoSurf produces high-performance natural glycolipids that can be incorporated into cleaning products, as well as cosmetic or personal care products, such as moisturizers, antioxidants, skin-lightening creams, antiaging creams, and sunscreens. These eco-friendly surfactants are low cost, high in purity, and safe, reducing the need for chemical surfactants that are both potentially harmful to humans and more persistent in the environment. Maier's early SRP research on biosurfactant-metal interactions, which focused on microbial glycolipids, laid a foundation for current GlycoSurf endeavors.



Maier is a professor in the Department of Soil, Water, and Environmental Science at UA. Her work focuses on understanding the role of microorganisms in the environment, and exploring the application of microorganisms and their products to benefit human health and the environment. (Photo courtesy of Raina Maier)

An easier way to detect mercury in the environment

Former UC Berkeley SRP trainees Jay James, Ph.D., and Jeffrey Crosby, Ph.D., won first place in the energy and cleantech category at the 2014 UC Berkeley Startup Competition April 24, for their patented technology to detect mercury contamination in the environment. Based on their UC Berkeley SRP research, James founded [Picoyune](#) to provide accurate and reliable mercury monitoring for industrial and environmental applications.

The sensing company's technology was developed to replace current spectroscopic methods requiring costly laboratory instruments to measure mercury. The hand-held technology, based on a mercury-selective film that responds to mercury vapor, is sensitive, easy to use, and low cost.

From the lab to the cheese industry

UC Davis SRP researcher Ian Kennedy, Ph.D., and postdoctoral trainee Sudheendra Lakshmana, Ph.D., founded [SonanuTech](#), which was selected to be part of the Davis Roots mentoring program in April. Davis Roots is a nonprofit business accelerator that fosters the early development of new companies.

A longtime SRP-funded researcher, Kennedy developed miniaturized biosensors to enable researchers to easily detect toxins in environmental samples, such as soil. Through this research, Kennedy and Lakshmana developed an innovative technology that offers a range of public health possibilities for detecting pathogens in foods, infections in humans, markers of cancer, and DNA.

They are currently bringing this portable and accurate pathogen detection technology to cheese manufacturers. Cheesemaking relies on bacterial cultures, but bacteriophages, viruses that can infect bacteria, can ruin the process, leading to significant financial losses for the industry. Their technology offers a new, faster test for the presence of harmful bacteriophages.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

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Before transitioning, full time, to the position of Picozyme's CEO, James was a Ph.D. student, then postdoctoral fellow, in the Department of Mechanical Engineering at UC Berkeley. (Photo courtesy of Jay James)



Kennedy, professor in the Department of Mechanical and Aerospace Engineering at UC Davis, specializes in biosensors based on nanomaterials. He is applying new and emerging technologies to implement bioassays with improved speed and sensitivity, compared to conventional methods. (Photo courtesy of Ian Kennedy)

NIEHS fellows earn honors at NIH Postbac Poster Day

By Sheila Yong

Caitlin McDonough and Jessica Boni, current NIH post-baccalaureate (postbac) Intramural Research Training Award (IRTA) fellows at NIEHS, won Outstanding Poster awards May 1 at the 2014 Postbac Poster Day at the NIH main campus in Bethesda, Maryland.

The annual NIH Postbac Poster Day allows these young researchers to display the research they have been conducting at NIH, and at the same time develop their communication and networking skills. This year, more than 400 postbac and technical IRTA fellows from various NIH institutes and centers (ICs) participated

in the event. The posters were judged by panels of graduate students, postdoctoral fellows, clinical fellows, staff scientists, and staff clinicians. Posters that scored in the top 20 percent were acknowledged with the awards.

Most of the participants were from ICs in the Bethesda, Baltimore, and Frederick, Maryland, areas, but NIEHS Scientific Director Darryl Zeldin, M.D., was determined to have the presence of NIEHS felt at the event. “The poster day was a great opportunity for NIEHS postbac IRTAs to network with their colleagues at other ICs, which is why I encouraged them to participate in this event, and paid out of the Office of the Scientific Director for their travel,” he explained. Seven out of the 11 postbac IRTAs at NIEHS in Research Triangle Park, North Carolina, presented their research at this year’s event.

A head start in scientific research

The NIH Postbac IRTA program provides recent college graduates, who are planning to apply to graduate or professional school, with an opportunity to spend one or two years performing full-time research at NIH institutes. McDonough and Boni took full advantage of this opportunity to prepare themselves for their future careers.

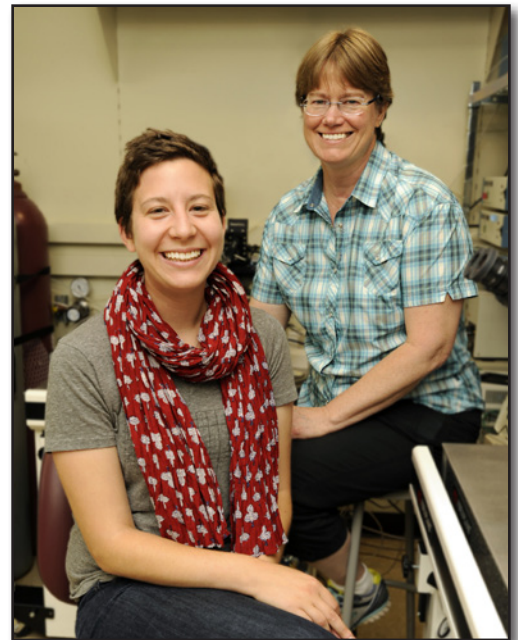
A native of Fuquay-Varina, North Carolina, [Boni](#) worked as an undergraduate intern during the summer of 2011 in the NIEHS Intracellular Regulation Group led by [David Miller, Ph.D.](#), where she first discovered her passion for scientific research. “I had such a wonderful experience that summer that I decided to take some time off before starting graduate school, and came back here as a postbac,” she said.

Boni’s experience at NIEHS has given her the confidence to begin her Ph.D. study this fall, when she will enter the Cell, Molecular, and Developmental Biology program at the University of Alabama at Birmingham. “Dr. Miller and everyone in my lab have been so supportive of my goals, and I have learned so much from all of them,” she said. “I can’t imagine a better way to be introduced to research, or learn how to be an independent researcher.”

[McDonough](#) found her calling in reproductive research through a more indirect route. After graduating from Beloit College in 2012, she spent a year performing research in conservation reproduction at the San Diego Zoo and the Smithsonian Conservation Biology Institute. “Although I loved this research, I realized it was not exactly what I wanted to do,” McDonough explained. While searching for new research opportunities, she came across the NIEHS Reproductive Medicine Group led by [Carmen Williams, M.D., Ph.D.](#), and the rest is history.



In the Miller lab, Boni, right, studies glucocorticoids, a class of steroid hormones that bind to the glucocorticoid receptor, which is expressed in almost all cells. She is specifically interested in how these hormones affect the blood-brain barrier and the potential issues they may cause in drug delivery to the brain. (Photo courtesy of Steve McCaw)



Research in the Williams group focuses on mechanisms of fertilization, using a mouse model system. In the fall, McDonough, left, will be entering a Ph.D. program at Syracuse University to study reproductive biology. “I will be very sorry to see her go off to graduate school, but am glad she is pursuing her dream career,” Williams said. (Photo courtesy of Steve McCaw)

In the Williams lab, McDonough found mentors who allowed her to try new things, encouraged her to be independent, and challenged her to achieve her fullest potential. “The highlight of my experience has been working with people who share my passion and interest for reproduction research,” she said.

Williams is impressed with McDonough’s performance in her lab. “Caitlin is absolutely outstanding in her ability to perform highly technically challenging experiments, in her drive to understand scientific questions, and in her intellectual rigor and curiosity,” she said.

Williams readily acknowledged the contributions of other members of her group to the quality of the mentoring experience. “Postdoc Miranda Bernhardt, Ph.D., has been Caitlin’s mentor this whole year and is completely responsible for Caitlin’s being able to accomplish so much.”

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Inositol Signaling Group.)

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Science Notebook


Kunkel elected to American Academy of Arts and Sciences

By Eddy Ball

This fall, NIH distinguished lead researcher Thomas Kunkel, Ph.D., will join fellow members in the 2014 class of the [American Academy of Arts and Sciences](#), at an induction ceremony Oct. 10-11 in Cambridge, Massachusetts.

Kunkel is one of seven new members of the group's Cellular and Developmental Biology, Microbiology, and Immunology Section. At NIEHS, he joins the late Scientific Director and Nobel Laureate Martin Rodbell, Ph.D., who became a member in 1993.


In their award letter to Kunkel, Chair of the Board Don Randel, Ph.D., and Chair of the Academy Council Diane Wood, J.D., congratulated Kunkel on his election. "This award signifies the high regard in which you are held by leaders in your field and members throughout the nation."



Linked video:

[Watch as Kunkel describes his research at NIEHS \(03:32\)](#)

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"This honor is truly a milestone in Tom's outstanding career," said NIEHS and NTP Director Linda Birnbaum, Ph.D. "It also says a great deal about the quality of scientific research at NIEHS, and I think it's more than fair to say that we all feel privileged to be his colleagues."

A driving force in molecular genetics and structural biology

Kunkel leads the [DNA Replication Fidelity Group](#) within the Laboratory of Structural Biology (LSB) and Laboratory of Molecular Genetics. During his 16-year tenure as the head of LSB, Kunkel oversaw the lab as it grew to include resource facilities to help provide further insight into how environmental exposures impact human health. LSB uses an integrated approach to investigate macromolecular structures at the atomic level, by combining biochemical and genetic approaches in conjunction with the lab's core research facilities.



AMERICAN ACADEMY
OF ARTS & SCIENCES



In addition to his accomplishments as a scientist, Kunkel has been a respected mentor of trainees over a career at NIEHS spanning 32 years. Under his leadership, LSB became one of the first labs implementing the dual mentoring program, to help postdoctoral fellows become more competitive in a changing job market. (Photo courtesy of Steve McCaw)

Kunkel came to NIEHS in 1982. Over his more than three decades of research on DNA replication, he has published nearly 340 papers in peer-reviewed journals, mentored an impressive group of accomplished scientists, and received a number of prestigious awards for his research. He has also served on several committees, including the Tenure Track Advisory Committee.

In addition to honors from professional organizations, Kunkel was selected as NIEHS Scientist of the Year in 2005, and won Paper of the Year in 2004, 2007, 2008, and 2009. When the NIH celebrated scientific discoveries made at the NIH over the previous two decades, among the 20 most cited papers by NIH investigators were two authored by him. Papers from Kunkel's group are routinely recognized as NIEHS papers of the month and papers of the year by the NIEHS Office of the Scientific Director.

Among Kunkel's many honors include his selection as chair of several Gordon Research Conferences, an Environmental Mutagen Society Award for Basic Research, and the Mutation Research Award. He received an honorary doctoral degree from Umeå University in 2007 for his identification of the DNA polymerase that replicates the leading strand of the eukaryotic nuclear genome.

In 2011, Kunkel was promoted to the rank of Distinguished Investigator, one of the highest honors the NIH awards to its scientists and one that only an estimated two to three percent of NIH scientists ever achieve during their careers (see [story](#)). He has developed several novel experimental approaches for investigating DNA replication and is considered one of the world's leading experts in the field.

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Understanding organ development

By Robin Arnette

For a mouse embryo to develop properly, many molecular events must occur within its body. Scientists have identified some of the steps, but one developmental biologist wants to fully understand the transition from endoderm, an early embryonic cell layer, to fully-functioning organs, a process known as differentiation.

Using a combination of real-time imaging and snapshot-style evaluation of organ differentiation, [Christopher Wright, D.Phil.](#), studies what happens as the pancreas develops in a mouse embryo. He believes that studying cell fate in mice will help researchers create cell-based therapies that combat human disease, such as diabetes and pancreatic cancer. Wright discussed his work May 6 as part of the NIEHS Distinguished Lecture Series. NIEHS Laboratory of Respiratory Biology lead Anton Jetten, Ph.D., hosted the seminar.

Cultivating every art and science

Members elected to the Academy are a select group of today's innovative thinkers in every field and profession, including more than 250 Nobel and Pulitzer Prize winners. Founded in 1780 by John Adams and James Bowdoin, the Academy's list of members reads like a Who's Who of American and world history. They range from Benjamin Franklin, Thomas Jefferson, and Charles Darwin to John Kennedy, Jonas Salk, and Nelson Mandela.

Kunkel is among a small group of current NIH researchers honored by election to the Academy and one of just three elected this year.

Other contemporary members include Duke University Nobel Laureate Robert Lefkowitz, M.D., Sir Paul McCartney, and Hillary Rodham Clinton. NIEHS grantee Michael Kastan, M.D., Ph.D., executive director of the Duke Cancer Center, is also a part of the class of 2014.

Growing in 3-D

The pancreas is a glandular organ with two functions — it produces hormones, such as insulin, that circulate in the bloodstream, as well as digestive enzymes that flow into the small intestine. Wright said that one of the most important recent discoveries was that the pancreas doesn't grow like the kidneys or lungs in an outward-branching formation with new growth at the ends of the epithelium. Instead, it grows from a complex meshwork of epithelial tubes, at the interior, middle, and exterior, simultaneously.

Wright explained that pancreatic and duodenal homeobox gene 1 (Pdx1) and pancreas specific transcription factor 1a (Ptf1a) are among the most critical early-acting transcription factors that drive pancreas development. Researchers have used knowledge of the regulation of these genes in attempts to culture beta cells, the insulin-producing cells that are lost or dysfunctional in type 1 and type 2 diabetes. Unfortunately, none have been successful.

“When the stem cells are differentiated in flat culture conditions, they tend to pile up on each other without any sense of collaborative organization,” Wright said. “Since they are not in the proper three-dimensional context, the only thing we get is immature beta cells.”

New technology reveals pancreas development

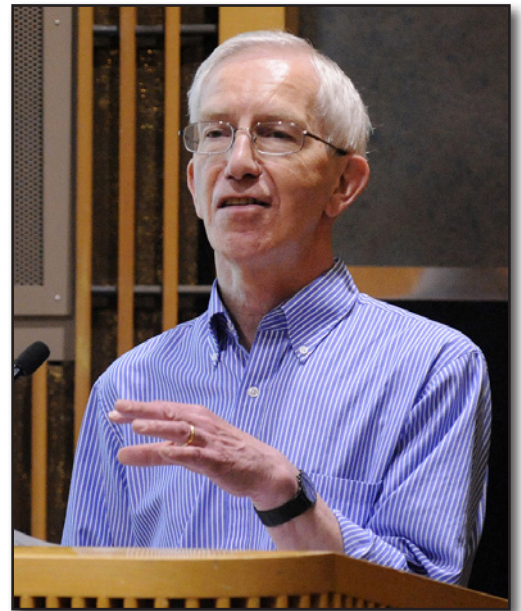
Using a microscope with real-time video imaging capability, Wright and his team made several discoveries, including that a third transcription factor called neurogenin 3 (Ngn3) was also needed for proper pancreatic growth and differentiation. It turns out that endodermal cells express Ngn3 at low levels, and when daughter cells that are committed to becoming pancreas beta cells split off from the parent cells, the daughters express high levels of Ngn3.

Communication between parent and daughter cells taking place in the epithelium, the birthplace of beta cells, was also discovered. In other epithelial tissues, such as the developing nervous system, it usually takes an hour or so for daughter cells to fully separate from their parent cells, but Wright's lab determined that daughter cells maintain a connection that may last 20 hours or more after cell mitosis, or division.

“We didn't know that such a close, prolonged parent-daughter cellular contact was possible before our real-time imaging made it inescapably clear,” Wright said, while showing the audience a short video clip of the process. “Perhaps young beta cells are instructing their parent cells to produce another beta cell in the next round of cell division.”



Wright holds several positions at Vanderbilt University, including director of the Program in Developmental Biology, professor in the Department of Cell and Developmental Biology, and the Louise B. McGavock Endowed Chair in Cell and Developmental Biology. (Photo courtesy of Steve McCaw)



Jetten also studies transcription factors as head of the NIEHS Cell Biology Group. (Photo courtesy of Steve McCaw)

Timing is everything

Another exciting finding to come from Wright's research was that he could completely transform an organ into a different organ. By using the antibiotic doxycycline to carefully time the production of Ptf1a, Wright was able to convert almost all of the stomach into pancreas tissue. Only the right timing and level of Ptf1a expression caused this remarkable organ conversion. At slightly later stages, when stomach differentiation had progressed further, no amount of doxycycline could induce the conversion, and stomach tissue formed as normal.

Wright's work has uncovered pivotal information about how cells differentiate into specific organs, and how the gene regulatory networks and intercellular signaling molecules control that development.

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Peer review panel evaluates draft NTP technical reports

By Ernie Hood

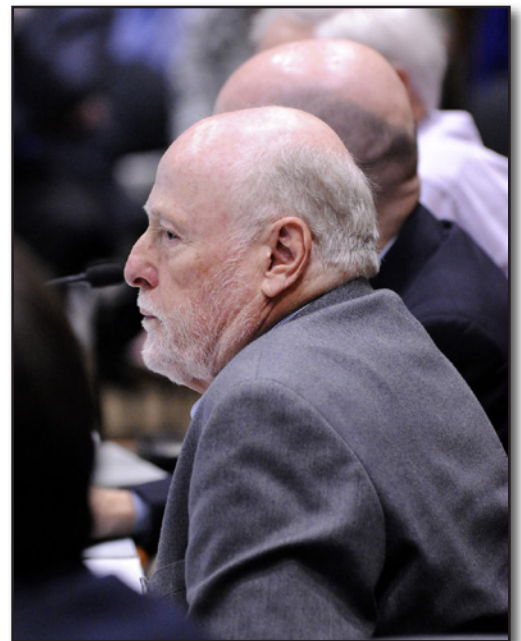
Draft NTP technical reports evaluating the carcinogenicity and toxicity of two dietary supplements, a water disinfection byproduct, and a metalworking fluid were peer reviewed May 22 by an [expert scientific panel](#).

NTP, an interagency program, conducts rodent toxicity and cancer studies on agents of public health concern to identify potential human health hazards. The technical reports describe the methods, results, and NTP conclusions regarding levels of evidence for carcinogenic activity under the specific conditions of each study.

Green tea extract

Green tea extract (GTE) is a commonly used dietary supplement in the U.S., marketed for its potential health benefits, such as increasing metabolism, fighting cancer, boosting the immune system, and promoting cardiovascular health. A component of GTE, epigallocatechin gallate, was originally nominated by the National Cancer Institute (NCI) for testing due to the lack of available chronic toxicity and carcinogenicity data. Ultimately, NTP chose to study GTE because there is more human exposure to the extract than to the nominated component. After analyzing several lots of commercially available GTE, NTP selected one GTE preparation for testing.

The panel accepted the draft NTP conclusions of no evidence of carcinogenic activity of GTE in male and female rats and in male mice. They also recommended a conclusion of no evidence of carcinogenic activity in female mice, instead of the draft NTP conclusion of equivocal evidence.



Hillary Carpenter III, Ph.D., a toxicologist retired from the Minnesota Department of Health, chaired the peer-review meeting. (Photo courtesy of Steve McCaw)

Indole-3-carbinole

Indole-3-carbinole is a dietary supplement sold alone or in combination with other herbals or vitamins. It is marketed as a cancer prevention agent, as well as for its health benefits, such as detoxifying the liver and boosting the immune system. NCI nominated indole-3-carbinole for study based on its occurrence in natural products such as cruciferous vegetables, including broccoli, Brussels sprouts, cauliflower, and kale, and its potential use as a breast cancer chemoprotective agent, to protect healthy tissue from the toxic effects of anticancer drugs.

The panel accepted the draft NTP conclusions of no evidence of carcinogenic activity in male rats and female mice, some evidence in female rats, and clear evidence in male mice.

Cimstar 3800

Cimstar 3800 is a semi-synthetic metalworking fluid used in machining automotive parts and other materials. The National Institute for Occupational Safety and Health nominated it for study based on a high potential for occupational exposures and the absence of toxicity or carcinogenicity studies.

The panel accepted the draft NTP conclusions of equivocal evidence in male and female rats, no evidence in male mice, and some evidence in female mice.

Bromodichloroacetic acid

Bromodichloroacetic acid (BDCA) is a member of the haloacetic acid family of drinking water disinfection by-products, formed when disinfectants such as chlorine or ozone are used in water treatment plants. It was nominated for study by the U.S. Environmental Protection Agency and the American Water Works Association Research Foundation, based on widespread human exposure in drinking water and lack of toxicity and carcinogenicity studies.



During the discussion of the draft NTP technical report on bromodichloroacetic acid, Robert Sills, D.V.M., Ph.D., chief of the Cellular and Molecular Pathology Branch, noted that brain tumors such as gliomas are rare in rodents, and that their contribution to the overall cancer burden is similar to humans, about 1-2 percent. (Photo courtesy of Steve McCaw)



For the benefit of those new to the NTP peer-review process, NTP toxicologist Chad Blystone, Ph.D., provided background information on the technical reports and the overall process, including the format of the peer review. (Photo courtesy of Steve McCaw)



Panel member Gary Perdew, Ph.D., of Penn State University, right, asked the NTP scientists many cogent questions during the discussions of the four draft NTP technical reports. (Photo courtesy of Steve McCaw)

The panel accepted the overall draft NTP conclusions of clear evidence of carcinogenic activity based upon a variety of neoplasms occurring in male and female rats and male and female mice.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



NTP pathologist Susan Elmore, D.V.M., explained the differences between the older and newer methods used by NTP pathologists to review uterine tissue sections. While the original transverse sectioning method remains in use, the newer residual longitudinal sectioning method has been used in six NTP studies so far, including three of the four studies being peer reviewed at the meeting — green tea extract, indole-3-carbinol, and Cimstar 3800. (Photo courtesy of Steve McCaw)



NTP toxicologist Daniel Morgan, Ph.D., was the study scientist for the draft NTP technical report on Cimstar 3800. (Photo courtesy of Steve McCaw)



NTP toxicologist Michael Wyde, Ph.D., study scientist for the indole-3-carbinole study, left, and NTP pathologist Ronald Herbert, D.V.M., Ph.D., right, answered questions from the peer-review panel. (Photo courtesy of Steve McCaw)



Panel member Jon Mirsalis, Ph.D., of SRI International in Menlo Park, California, concurred with the conclusions in one of the draft NTP technical reports. (Photo courtesy of Steve McCaw)

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Statistical geneticist Dmitri Zaykin tenured

By Robin Arnette

NIEHS statistical geneticist [Dmitri Zaykin, Ph.D.](#), left the tenure-track ranks April 7, when the National Institutes of Health Central Tenure Committee voted to award him tenure. He is a senior researcher in the NIEHS Biostatistics Branch.

Zaykin is interested in uncovering relationships between genetic variation and phenotypic traits, using statistical methodology. The techniques that he and his group develop are also applicable to studies involving epigenetic effects of exposures, metabolomics, and differential gene expression. He said he's always been fascinated with the interface between mathematics, statistics, and biology.

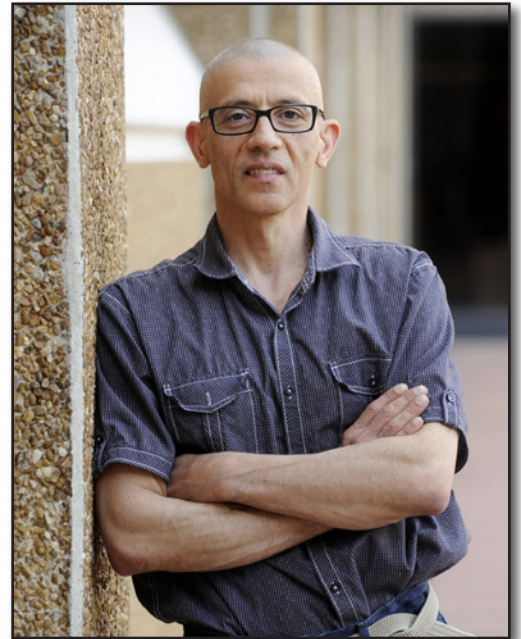
“Statistical genetics is interwoven with population genetics and evolutionary theory, and it stands alone as an exciting field of science, rather than being simply a category of biostatistics concerned with genetic data,” Zaykin said.

His work has led to dozens of peer-reviewed journal articles that delve into the roles of genetic and environmental susceptibility factors in human disease. NIEHS Biostatistics Branch head Clarice Weinberg, Ph.D., said Zaykin's expertise in statistics, population genetics, and genetic epidemiology has helped to make NIEHS a leader in the development of methods for studying environmental health.

“We are extremely fortunate to have Dmitri on board,” Weinberg said. “He uses creative approaches to finding real signals amid the huge amount of noise generated by emerging methods in biotechnology.”

Zaykin completed a master's-equivalent degree in biology and population genetics from Far Eastern State University, Vladivostok, Russia, and a doctorate in biomathematics from North Carolina State University. He held research positions at GlaxoSmithKline before joining NIEHS in 2004.

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In his spare time, Zaykin likes listening to classical music, reading, and weightlifting. (Photo courtesy of Steve McCaw)

Small fish may offer big opportunities for future toxicity testing

By Catherine Sprinkle

Scientists from around the world met May 5-6 at North Carolina State University (NCSU) in Raleigh, to consider the key role small fish and fish embryos may play in toxicity testing. Thousands of chemicals are used in industry, agriculture, and consumer products every day, and hundreds more are being developed every year. Yet little is known about how they affect human health. Scientists typically use mice and rats to identify potential health risks of chemicals, but researchers are now considering using other species that would make testing quicker and easier.

International gathering meets local collaboration

The [Collaborative Workshop on Aquatic Models and 21st Century Toxicology](#) drew nearly 150 scientists from the U.S., Canada, Europe, and Asia to discuss the use of small fish or fish embryos in testing to assess chemical safety. A diverse group of scientists from the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods ([NICEATM](#)), NCSU, Duke University, the U.S. Environmental Protection Agency, and the U.S. Food and Drug Administration (see sidebar), organized the workshop.

[Daniel Solomon, Ph.D.](#), dean of the NCSU College of Sciences, welcomed attendees to the new and technologically advanced [James B. Hunt Jr. Library](#) on the NCSU campus. Solomon noted the large number of Research Triangle, N.C., area attendees at the workshop in his opening remarks. “Despite the athletic rivalries that exist between our local universities, there are strong collaborations among the researchers, including those working with zebrafish,” he said.

NICEATM Director [Warren Casey, Ph.D.](#), also welcomed the attendees and remarked that this gathering was part of a larger effort to rethink traditional approaches to toxicology. “We now have the technology to make substantial changes in the way toxicology testing is conducted.”

Research, practical advice, data use, and awards

More than 20 scientific talks were given during the two-day workshop, many of them by NIEHS grantees. Presentations included descriptions of research studies and results, practical advice on conducting toxicity



In his welcoming remarks, Solomon noted NCSU's strong tradition in biological research, and efforts by NCSU scientists to strengthen the interface between research and medicine. (Photo courtesy of Catherine Sprankle)



Casey provided an overview of how small fish might provide an alternative model for toxicity testing. (Photo courtesy of Catherine Sprankle)

Workshop organizing committee

NIEHS: Casey; Christopher Weis, Ph.D.; Mamta Behl, Ph.D. (contractor); Jonathan Hamm, Ph.D. (contractor)

NCSU: Seth Kullman, Ph.D.; Carolyn Mattingly, Ph.D.; Antonio Planchart, Ph.D.

Duke University: David Hinton, Ph.D.

Environmental Protection Agency: Tamara Tal, Ph.D.

National Center for Toxicological Research, U.S. Food and Drug Administration: Jyotshna Kanungo, Ph.D.

studies using small fish and fish embryos, and use of toxicity data derived from aquatic species in drug development and regulatory compliance.

A poster session May 5 allowed attendees to interact informally and learn about other research being conducted. The organizing committee recognized junior researchers from NCSU, Oregon State University, and the University of South Carolina for outstanding presentations.

Participants highlight next steps

The conference concluded May 6 with a discussion session. Workshop participants noted that the suitability of small fish species for toxicity testing, particularly their practical advantages, needs to be brought to the attention of other audiences, including industry, regulators, scientists in other disciplines, and the general public.

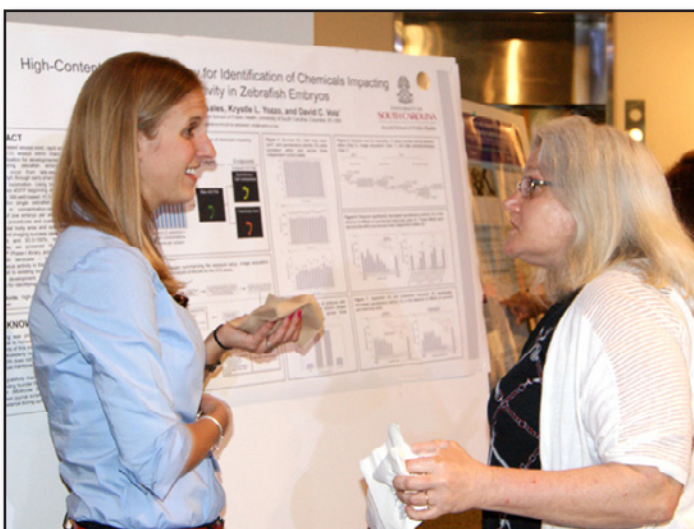
Topics identified for further exploration included the effective application of fish study data for better understanding of chemical safety, and integration of fish data with complementary information from other types of toxicity studies. Other needs included clarification of the relationship between chemical treatment, uptake and metabolism, and the observed effects in fish models.

Attendees agreed that the research presented at the workshop was important and of high quality, and that the event provided a valuable opportunity for researchers within and outside the field of toxicology to share insights on the potential role of small fish and fish embryos in the future of toxicology.

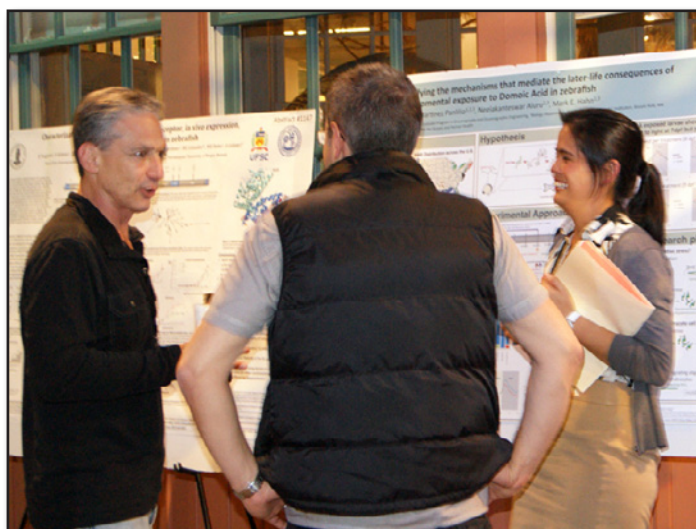
A summary and full report of the workshop will be developed and posted on the workshop Web page, along with presentations and poster abstracts.



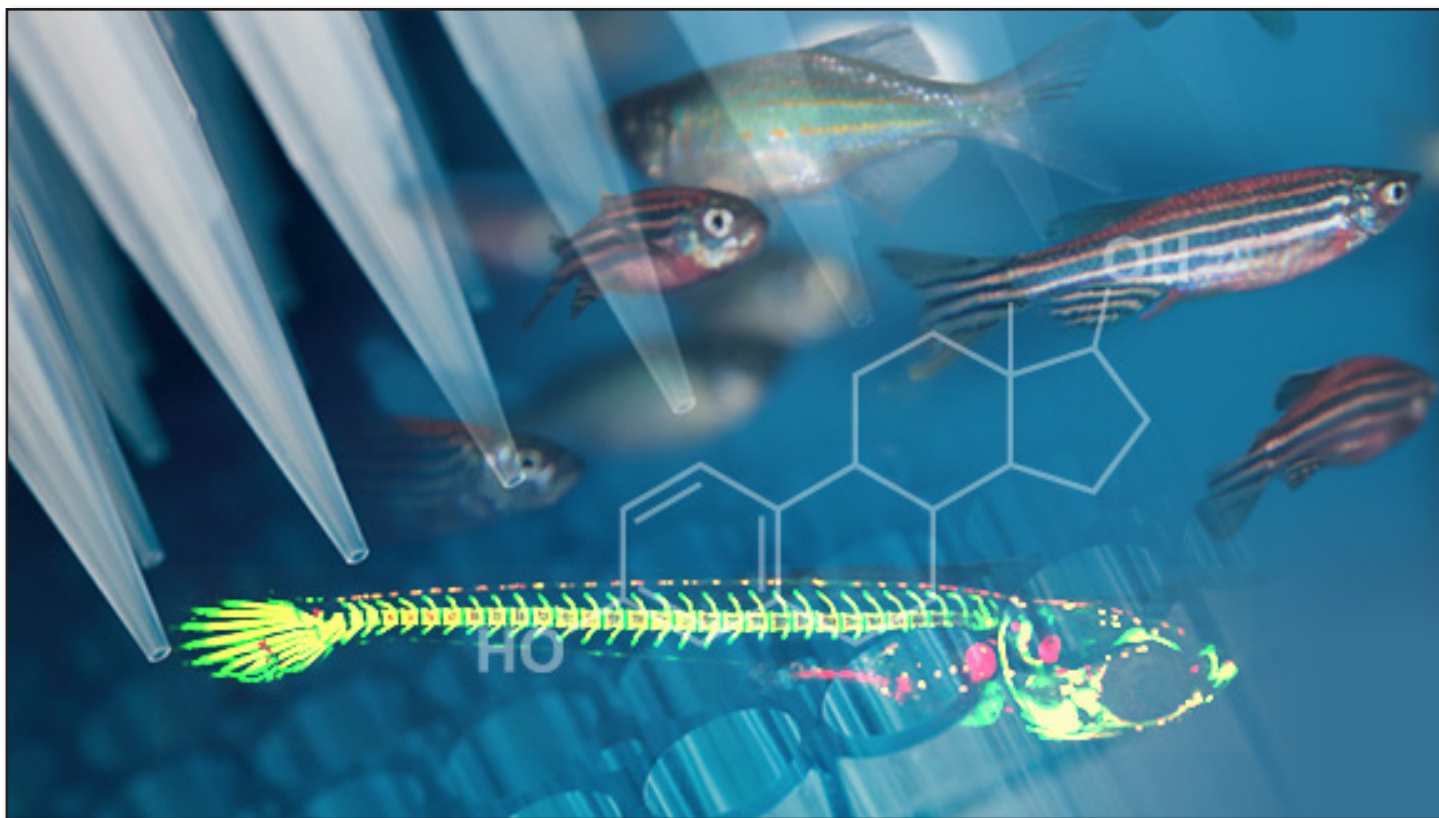
Organizing committee members Mattingly, left, and Behl found a moment to relax during a break. (Photo courtesy of Catherine Sprankle)



Tara Raftery, left, a graduate student working with NIEHS grantee David Volz, Ph.D., at the University of South Carolina, answered many questions from attendees during the workshop's poster session. Raftery's poster was recognized as one of three outstanding student presentations at the workshop. (Photo courtesy of Catherine Sprankle)



The poster by Jennifer Panlilio, right, a graduate student at Woods Hole Oceanographic Institution, sparked a discussion with workshop presenters Jeff Bronstein, M.D., Ph.D., of the University of California, Los Angeles, left, and Matthew Winter, Ph.D., of the University of Exeter. (Photo courtesy of Catherine Sprankle)



(Catherine Sprankle is a communications specialist with ILS Inc., support contractor for NICEATM.)

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Cell signaling researcher explores the frontiers of therapeutic potential

By Eddy Ball

NIEHS lead researcher [Stephen Shears, Ph.D.](#), opened his May 12 talk by describing its title as provocative. The presentation, “Cell Signaling by Inositol Pyrophosphates: Therapeutic Potential?” was part of the Laboratory of Signal Transduction Seminar Series, hosted by Perry Blackshear, M.D., D.Phil.

Although posed as a question, the fact that Shears could speak with confidence about therapeutic potential marks an important shift in thinking about inositol pyrophosphates (PP-IPs) and the enzymes, or kinases, that synthesize them. The PP-IPs are specialized members of the inositol phosphate (IP) cell signaling family.

New work by Shears’ group and his collaborators has suggested that PP-IPs represent a target for therapy, to address several conditions triggered internally or by environmental exposures, such as viral infection, cancer, inflammation, diabetes, obesity, and aging-related diseases. Nevertheless, it is only in the past few weeks that anyone from the pharmaceutical industry has apparently paid much attention to PP-IP signaling.

“It [the title of this talk] was prompted by two communications I’ve had over the past three weeks or so [about the group’s latest [paper](#), published online in April],” Shears said. “One was something I’d never even heard of before — the [Science-Business eXchange](#) — which is a kind of gateway between scientific communications and the pharmaceutical industry.... And then a pharmaceutical company [[Ono Pharma USA](#)] came here a couple of weeks ago to talk about IP7 kinase [IP7K] and its possible therapeutic potential.”

Moving from basic mechanisms to therapeutic targets

In the course of a publishing career that began in 1979, Shears has authored and co-authored nearly 150 papers, most of them studies on some aspect of IP metabolism that he and his colleagues have been the first to describe using biochemical, cell biological, and, more recently, structural approaches. As Shears explained, the synthesis of substrate analogues to inhibit IP kinases (IPKs) was complicated by chemical and electrical properties that made purification especially time-consuming.

An important step in drug discovery is to solve the crystal structure of suitable target enzymes. Then, drugs can be rationally designed to block the substrate-binding site. However, this is an especially challenging task with IPKs. When Shears and his group finally solved the structure of IP7K, they found a tight, highly specific binding pocket and a very unusual surface-mounted substrate binding site that acts as a funnel into the binding pocket.

“What we think is that this is a more flexible site, less specific, that acts to capture the substrate from the bulk phase and then transport it into the binding pocket,” Shears said. One of the synthetic PP-IP analogues that Shears’ collaborators synthesized was found to inhibit IP7K by blocking the substrate-capture site, rather than directly interfering with the catalytic pocket of the enzyme. Looking to work ahead, he suggested, “Maybe we can rationally design an inhibitor that is more hydrophobic and can get inside to actually inhibit the kinase.”

The Shears group is also collaborating with scientists at the University of North Carolina at Chapel Hill, to test other synthetic substrates for manipulating IP7K activity with high-throughput screening.

Citation: Wang H, Godage HY, Riley AM, Weaver JD, Shears SB, Potter BV. 2014. Synthetic inositol phosphate analogs reveal that PPIP5K2 has a surface-mounted substrate capture site that is a target for drug discovery. Chem Biol; doi:10.1016/j.chembiol.2014.03.009 [Online 23 April 2014].

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“IP7 kinases are involved in stimulating interferon transcription in response to viral infection,” Shears told the audience. “The [signaling] pathways that are activated by viruses are also activated in metabolic inflammation, too. So these may also be relevant in diabetes and obesity.”
(Photo courtesy of Steve McCaw)

Fast test for measuring DNA repair

By Anne Trafton

A new test developed by an NIEHS-funded research team at the Massachusetts Institute of Technology (MIT) can analyze four types of DNA repair capacity simultaneously. This test could help determine an individual’s risk of developing cancer and help doctors predict how a given patient will respond to chemotherapy drugs.

Previous tests have been able to evaluate only one DNA repair system at a time. Described in a [paper](#) published in the journal Proceedings of the National Academy of Sciences, the test of all four systems takes less than 24 hours.

Damage to DNA

DNA is under constant attack from many sources, including environmental pollutants, ultraviolet light, and radiation. Cells have several major DNA repair systems that can fix this damage, which may lead to cancer and other diseases if not repaired properly.

The effectiveness of these repair systems varies greatly from person to person. Scientists believe that these differences may explain why some people get cancer, while others exposed to similar DNA-damaging agents do not.

Measuring each repair system takes expertise, time, and is labor-intensive, said Zachary Nagel, Ph.D., an MIT postdoctoral researcher and lead author of the paper. “What we wanted to do was come up with one way of measuring all DNA repair at the same time, so you have a single readout that’s easy to measure,” he said.

The research team, led by [Leona Samson, Ph.D.](#), used the new test to measure DNA repair in a type of human blood cell. They found huge differences among samples from 24 healthy volunteer donors, especially in one repair system where cells from some volunteers were more than 10 times more efficient than those from others.

“None of the cells came out looking the same. They each have their own spectrum of what they repair well and what they don’t repair well,” said Samson, who is an [NIH Pioneer](#) awardee.

Future uses may predict risk, screen treatments

Scientists have identified links between DNA repair and neurological, developmental, and immunological disorders. But useful, predictive tests for DNA repair have not been developed, largely because it has been impossible to rapidly analyze several different types of DNA repair capacity at once.

Samson’s lab is now working on adapting the new test. They are researching whether the test could be used to identify people who are at higher risk for diseases and potentially enable prevention or earlier diagnosis. Other potential uses include predicting a patient’s response to chemotherapy drugs, which often work by damaging the DNA of cancer cells, and determining how much radiation treatment a patient may tolerate.

Another important application for this test could be studying fundamental biological processes, such as how cells recruit backup repair systems to fill in when another pathway is overwhelmed, says [Samuel Wilson, M.D.](#), head of the NIEHS DNA Repair and Nucleic Acid Enzymology Group.



Nagel said the new test could be used to screen for new drugs that inhibit or enhance DNA repair. Inhibitors could target tumors to make them more susceptible to chemotherapy, while enhancers could help protect people who have been accidentally exposed to DNA-damaging agents, such as radiation. (Photo courtesy of the Samson Lab)



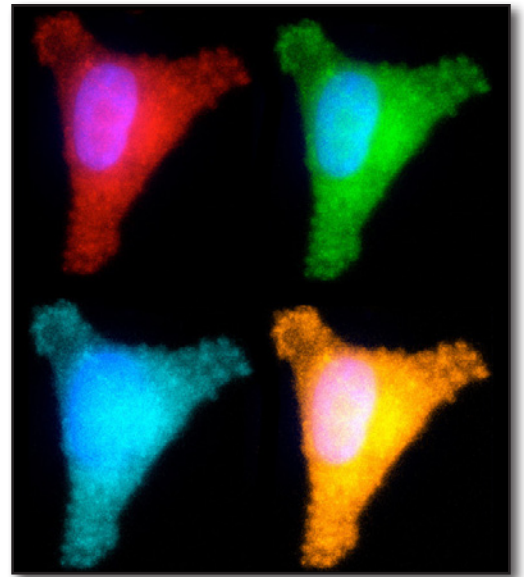
Samson is an Uncas and Helen Whitaker Professor, American Cancer Society Research Professor, and a member of the MIT Department of Biological Engineering, Department of Biology, Center for Environmental Health Sciences, and David H. Koch Institute for Integrative Cancer Research. (Photo courtesy of the Samson Lab)

“There’s an opportunity to use these multiplexed plasmids in biological assays where several repair pathways can be probed at the same time, offering a very advanced tool to allow us to make much better interpretations about the repair status of a cell,” said Wilson, who was not part of the research team.

Citation: Nagel ZD, Margulies CM, Chaim IA, McRee SK, Mazzucato P, Ahmad A, Abo RP, Butty VL, Forget AL, Samson LD. 2014. Multiplexed DNA repair assays for multiple lesions and multiple doses via transcription inhibition and transcriptional mutagenesis. *Proc Natl Acad Sci U S A* 111(18):E1823-E1832.

(This story was adapted from an [article](#) by Anne Trafton, a writer with MIT News, the MIT News Office publication.)

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MIT biological engineers have developed a way to test several different DNA repair pathways in one cell. In each of these images, the cell is producing a different fluorescent protein, indicating whether it has successfully repaired one of four different types of DNA damage. (Image courtesy of MIT News)

Scientists study impacts of climate change on public health

By Audrey Pinto

The NIEHS Partnerships for Environmental Public Health hosted a webinar April 25 highlighting the research of two NIEHS-funded scientists, Antonella Zanobetti, Ph.D., and Julia Gohlke, Ph.D., who are developing methods to assess and quantify the role of climate change on human health.

In the NIEHS [2012-2017 Strategic Plan](#), climate change was identified as an emerging environmental threat to human health (see [story](#)), and an area that needed further research to help inform policy. [Zanobetti](#), senior research scientist at the Harvard School of Public Health, and [Gohlke](#), Professor at the University of Alabama School of Public Health, are attempting to fill the data gaps.

Quantifying health effects

“Currently, the most pressing need in environmental health research is to focus on estimating and assessing the potential health effects of climate variability on public health,” explained Zanobetti.

To this end, she and her colleagues investigated the short-term and long-term health effects of weather exposure on nearly 25 million people, in 135 U.S. cities, older than 65, with predisposing diseases.

Zanobetti’s group linked Medicare records to data from several sources, including the National Oceanic and Atmospheric Administration, 2000 census, and [2001 National Land Cover Dataset](#). They then examined hospital admissions and causes of death from 1985 through 2006.

“We investigated the long-term effects of exposure to summertime temperatures on survival among adults who were hospitalized with heart disease, respiratory illness, and neurological disorders during the study period,” Zanobetti said.

Climate variability affects certain populations

Zanobetti and colleagues found measurable increases in mortality associated with increased summer temperatures among persons older than 65 who had been hospitalized with chronic conditions, such as congestive heart failure and diabetes. The mortality rates were also higher for nonwhite women and those living in poverty. There was a greater chance of survival for individuals with college educations and for individuals living in areas with more green space.

“Our findings contribute important information for targeting and implementing effective public health programs during extreme hot and cold weather events, for elderly populations living in cities with little or no green space,” she concluded.

Community collaboration

In a health study of urban and rural communities, Gohlke collaborated with the Friends of West End Inc. in Birmingham, Alabama, and the [West Central Alabama Community Health Improvement League](#), which serves several Alabama rural counties, to investigate the impact of extreme heat events on preterm births (PTB) and nonaccidental deaths (NAD).

“Our initial aims were to establish strong partnerships across community organizations and local health departments in urban and rural communities in Alabama, establish environmental health priorities, and assess health outcomes associated with extreme heat events using birth and death records from 1990–2010,” Gohlke said.

A unique tool for studying heat-related effects

Using birth and death records, and a unique exposure metric that measures heat wave days at the ZIP code level — the National Land Data Assimilation System Phase 2 ([NLDAD-2](#)) — Gohlke and colleagues designed a study to examine associations between PTB and NAD in extreme heat conditions.

Gohlke reported, “We found that relative, average, and maximum heat waves were associated with increased PTB and NAD, and the association between heat waves and NAD are greater in urban areas.”

“We believe our findings suggest that developing tangible adaptation strategies to address community priorities may be the most effective approach to climate change adaptation,” Gohlke said in closing.

Citation: [Zanobetti A](#), [O’Neill MS](#), [Gronlund CJ](#), [Schwartz JD](#). 2012. Summer temperature variability and long-term survival among elderly people with chronic disease. *Proc Natl Acad Sci U S A* 109(17):6608-6613.

(Audrey Pinto, Ph.D., is technical editor for the NIEHS journal *Environmental Health Perspectives*.)

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*Zanobetti’s work was cited in [A Human Health Perspective on Climate Change](#), a 2010 report published by the journal *Environmental Health Perspectives* and NIEHS. (Photo courtesy of Antonella Zanobetti)*



Gohlke was a member of the Interagency Working Group on Climate Change and Health, which authored the 2010 [report](#). (Image courtesy of the University of Alabama at Birmingham)

Prenatal arsenic exposure and altered protein expression

By Sara Mishamandani

NIEHS-funded scientists reported changes in biological pathways, associated with prenatal inorganic arsenic exposure, in a [paper](#) selected as an Editor's Highlight in the June issue of the journal *Toxicological Sciences*. The research, led by Rebecca Fry, Ph.D., at the University of North Carolina at Chapel Hill (UNC), is the largest protein-based study of an arsenic pregnancy cohort to date. The work provides insight into the mechanisms linking early life exposure to arsenic with disease susceptibility later in life. It further identifies proteins and pathways that may help in uncovering biomarkers of arsenic exposure and, thus, disease risk.

“Health effects associated with exposure to environmental contaminants are determined by the exposure, as well as by how the individual responds to that exposure,” said Fry. “This study improves our understanding of the biological mechanisms underlying adverse health outcomes, particularly related to children’s health.”

Measuring changes in protein levels from arsenic exposure

Fry recently established the Biomarkers of Exposure to ARsenic (BEAR) cohort, a pregnancy cohort consisting of 200 mother-infant pairs residing in Gomez Palacio, in the Lagunera region of northern Mexico, where drinking water contains high levels of arsenic. Fry and her colleagues collected mothers’ urine, drinking water, and umbilical cord samples. Using arsenic levels found in the urine and drinking water as a guide, researchers then chose 50 mother-infant pairs, with varying levels of arsenic, for conducting the protein analysis.

Using a large-scale screen of protein levels, researchers identified 111 altered proteins in the cord blood of infants prenatally exposed to arsenic. Almost half of these proteins are regulated by tumor necrosis factor (TNF), which plays a critical role in inflammation, as well as cellular growth and development-related signaling.

“Using an analytical framework to target biological pathways associated with the altered proteins, we can pinpoint the master regulators of the response to arsenic exposure,” said Fry. “The identification of these key players, such as TNF, informs the mechanisms of disease and helps us target novel molecules for arsenic health effects research.”

Understanding differences in response to arsenic

Fry and her research team also observed differences in protein expression levels among infants exposed to arsenic. Of the 50 newborns, 30 were considered activators, exhibiting higher than average protein expression levels. The remaining 20, the repressors, displayed lower protein expression levels.

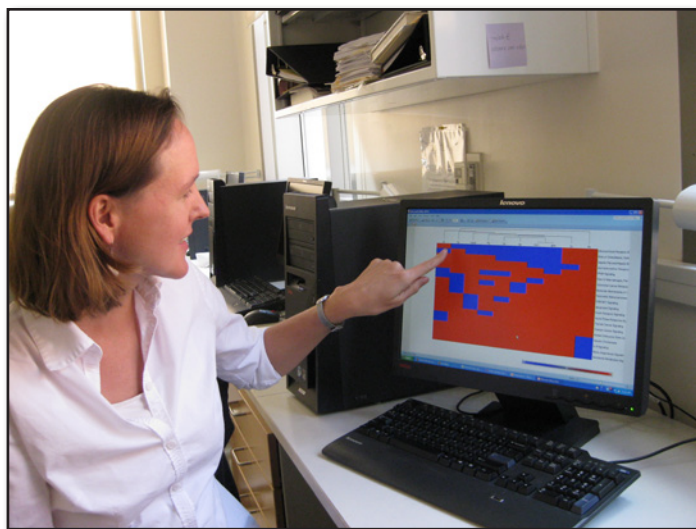
A relationship between increased maternal arsenic levels and decreased head circumference at birth was found in activator males. According to the authors, the relationship between prenatal arsenic exposure and head circumference may be linked to health effects later in life because, in general, there is a positive relationship between head circumference at birth and childhood cognitive ability.



Fry is an NIEHS 2010 Outstanding New Environmental Scientist awardee and a grantee with the UNC Superfund Research Program. She is an associate professor in the UNC Gillings School of Public Health Department of Environmental Sciences and Engineering. (Photo courtesy of Rebecca Fry)

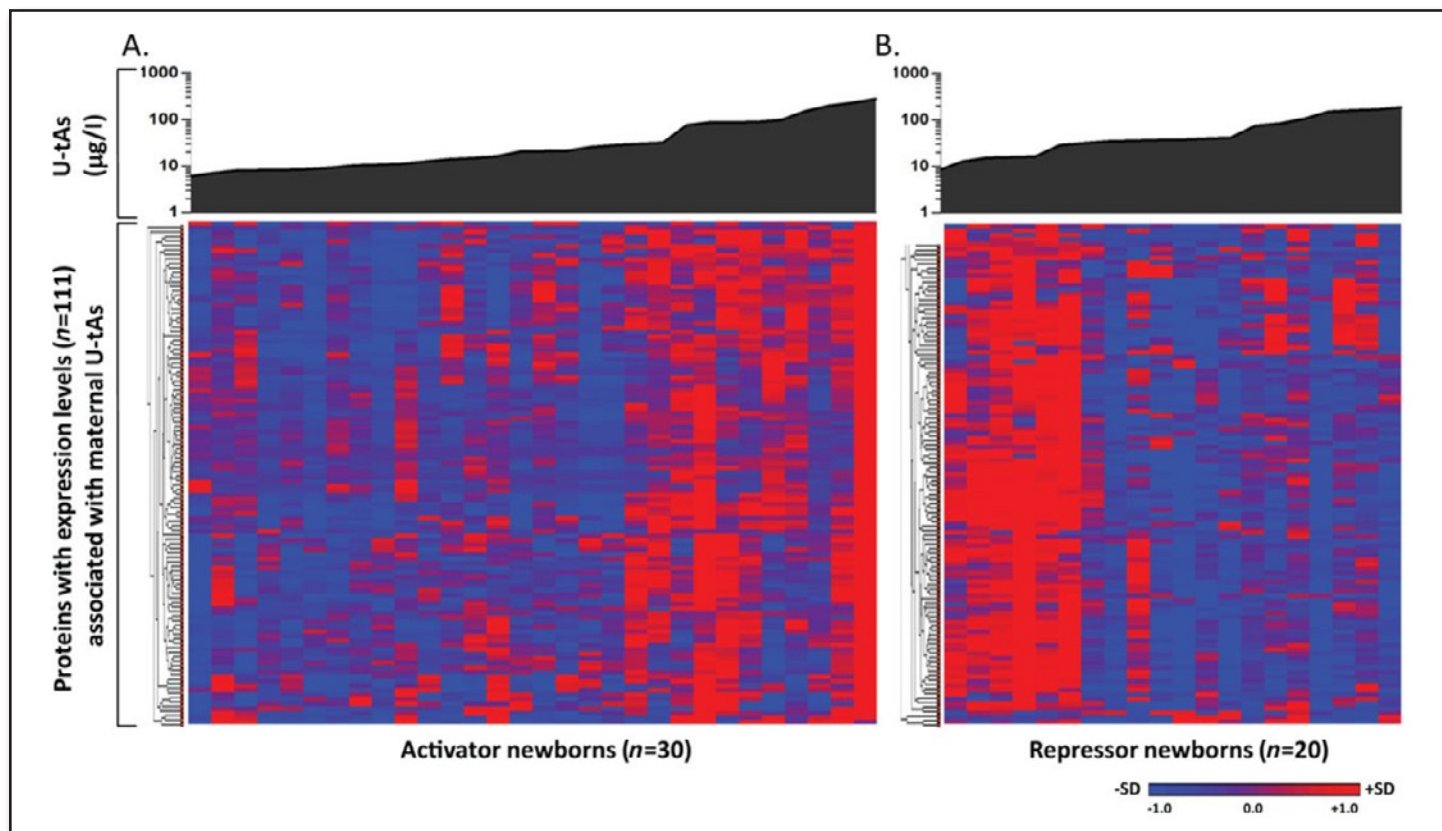
Of potential interest to this study, research based in Torreon, Mexico, a city neighboring Gomez Palacio, demonstrated that boys and girls differed in terms of cognitive deficiencies associated with arsenic exposure, with more cognitive deficiencies observed in boys than girls.

More than 100 million people worldwide are exposed to inorganic arsenic levels exceeding the World Health Organization recommended drinking water limit of 10 micrograms of arsenic per liter. Long-term exposure to arsenic can result in chronic health conditions, such as cardiovascular disease, diabetes, and cancer. Exposure to high levels of arsenic during pregnancy is also associated with risks to maternal and fetal health, and childhood exposure can bring adverse health effects later in life, including increased rates of lung, bladder, and liver cancers.



Fry uses systems toxicology to understand the molecular mechanisms by which early-life exposures to metals are associated with long-term health effects in humans. (Photo courtesy of the UNC Superfund Research Program)

The results of this study provide an important foundation for further understanding the relationship between prenatal arsenic exposure, protein response, and disease susceptibility. The identified proteins may also serve as novel targets for understanding arsenic-associated effects on fetal growth and disease later in life.



Researchers used heat maps to illustrate the relative expression levels of the 111 proteins associated with arsenic exposure in activator and repressor newborns. High relative expression is indicated in red and low relative expression is indicated in blue. As the level of maternal urinary arsenic (U-tAs) increased, activator newborn protein expression also increased, whereas repressor newborn protein expression decreased. (Image source: Bailey KA, et al. Toxicol Sci 139:328-337)

Citation: Bailey KA, Laine J, Rager JE, Sebastian E, Olshan A, Smeester L, Drobna Z, Styblo M, Rubio-Andrade M, Garcia-Vargas G, Fry RC. 2014. Prenatal Arsenic Exposure and Shifts in the Newborn Proteome: Interindividual Differences in Tumor Necrosis Factor (TNF)-Responsive Signaling. *Toxicol Sci* 139(2):328-337.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

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High-throughput toxicity screening produces human-relevant results

By Thomas Burns Jr.

Using *in vitro* and *in silico* testing in primary human cell systems, scientists reported in the May issue of the journal *Nature Biotechnology* bioactivity profiles for 776 unique and diverse chemicals with potential for human exposure. The use of a human-relevant system may provide a rapid and accurate screening method to prioritize chemicals for further toxicity testing or to identify new pharmaceutical activities.

“This is the first data manuscript in the field of high throughput toxicity screening [HTS] on such a large number of chemicals to be published in one of the *Nature* journals,” said Nicole Kleinstreuer, Ph.D., the paper’s lead author, who is now a contractor supporting the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). “It demonstrates the utility of HTS assays that use human primary cells to elucidate mechanisms of action and predict toxicities for a diverse set of chemicals.”

Limitations of traditional toxicity testing

Toxicity data on many chemicals do not exist. The study’s authors point out that it is difficult or impossible to test these chemicals for toxicity using traditional animal testing methods, because of the expense, time required, ethical concerns about animal testing, and problems with species extrapolation.

The researchers wanted to examine whether *in vitro* and *in silico* high throughput test methods, especially those using human cell and gene targets, could provide a viable alternative to such testing.

In vitro testing can provide human-relevant results

Scientists from the U.S. Environmental Protection Agency (EPA) tested 776 unique environmental and industrial chemicals, including pesticides, food additives, and pharmaceuticals. The researchers chose eight human primary cell systems, based on their sensitivity to specific drug mechanisms and adverse effects, and recorded 87 different measurements, resulting in 306,240 individual data points.



Kleinstreuer’s work with NICEATM seeks to increase the efficiency of toxicity testing by allowing resources for follow-up testing to be focused on the bioactivities of highest concern. (Photo courtesy of Steve McCaw)

Pharmaceuticals and pesticides were the most active chemicals, while fragrances and colorants, used in cosmetics and as food additives, proved to be the least active. Only eight percent of the chemicals were uniformly inactive, including a few known to be pharmaceutically active in humans — a finding that highlights both areas for further research as well as the potential need for additional endpoints of study.

Identifying chemicals with previously unknown mechanisms of action

The study's authors reported intriguing results of the cluster analysis. Researchers grouped chemicals that showed a similar endpoint profile, so that specific mechanisms of action could be inferred for each group. For example, analgesics, such as aspirin and the non-steroidal anti-inflammatory drugs Indomethacin and Celecoxib showed similar endpoint profiles, a finding that helped validate this approach.

A seemingly unrelated chemical, propyl gallate, a common cosmetic and food additive, also clustered with this group, suggesting that propyl gallate might have a similar mechanism of action as do the known analgesics. This finding illustrates the potential of this approach to shed light on as yet unrecognized toxicities or mechanisms of action for chemicals, based on profile similarities.

This work was conducted as part of the EPA [ToxCast](#) Program, which is a member of [Tox21](#), a federal consortium that includes NIEHS, NTP, EPA, the National Center for Advancing Translational Sciences, and the U.S. Food and Drug Administration. The goal of Tox21 is to develop predictive toxicity models and prioritization schemes based on data from alternative testing methods.

Citation: [Kleinstreuer NC, Yang J, Berg EL, Knudsen TB, Richard AM, Martin MT, Reif DM, Judson RS, Polokoff M, Dix DJ, Kavlock RJ, Houck KA. 2014. Phenotypic screening of the ToxCast chemical library to classify toxic and therapeutic mechanisms. Nat Biotechnol; doi:10.1038/nbt.2914 \[Online 18 May 2014\].](#)

(Thomas Burns Jr. is a contract writer with Tekrighter Scientific and Medical Writing Services in Wendell, North Carolina.)

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Investigating medications as a source of phthalate exposure

By Annah Wyss

In an NIEHS Epidemiology Branch seminar May 12, Sonia Hernandez-Diaz, M.D., Dr.P.H., associate professor of epidemiology at Harvard University, shared the evolution of her studies of potential phthalate exposure from some frequently prescribed medications, demonstrating how ingenuity and perseverance propel research forward.

Phthalates are a class of chemicals commonly used as plasticizers and solvents. In animal studies, phthalates have been associated with birth defects in offspring, namely male genital malformations, and [Hernandez-Diaz](#) said it was natural to suspect that similar effects in humans might result from exposure to phthalates in the environment.

“As a result of the wide use of phthalates, humans are exposed to phthalates via ingestion, absorption, and inhalation, and offspring can be exposed through *in utero* maternal exposure. So we began to wonder about medications as an exposure source,” she explained.

In particular, two common phthalates, diethyl phthalate (DEP) and dibutyl phthalate (DBP), are used in coatings of medications and supplements, to control the release of active ingredients. Hernandez-Diaz and colleagues, including [Allen Wilcox, M.D., Ph.D.](#), head of the NIEHS Reproductive Epidemiology Group, hypothesized that phthalates in medications taken by pregnant women might be associated with adverse health outcomes in offspring. In order to prove this hypothesis, researchers first had to determine which medications contained phthalates and investigate the exposure burden.

Exploring the exposure burden

Since no published list of medications containing phthalates existed, the group combed through product packaging, patents, and databases, and even contacted manufacturers and distributors directly. Through this systematic search, the team identified more than 110 products with phthalates. Approximately 50 prescription drugs and 65 over-the-counter medications and dietary supplements contained DEP or DBP, while more than 90 products contained other phthalates.

Having developed a list of medications containing phthalates, they next focused on estimating the U.S. population's exposure to phthalates via medications. Using data from the National Health and Nutrition Examination Survey ([NHANES](#)), which asked individuals about the prescriptions they took in the last 30 days and obtained urinary concentrations of 13 phthalate metabolites for a subsample, she found that those who had taken the drugs mesalamine, didanosine, omeprazole, and theophylline had higher concentrations of phthalate metabolites in their urine than those who did not. These medicines are used for a variety of conditions, including ulcerative colitis, HIV, dyspepsia, gastroesophageal reflux disease, and respiratory diseases, like asthma and chronic obstructive pulmonary disease.

To focus specifically on women of childbearing age, Hernandez-Diaz and colleagues then looked at data from the Environment and Reproductive Health ([EARtH](#)) Study. Similar to NHANES, women in the EARtH Study self-reported medication use and provided urinary samples. Again, women who took mesalamine or omeprazole had higher concentrations of phthalate metabolites in their urine than those who did not, though estimates were based on a limited number of users. Both the NHANES and EARtH Study results suggest that humans, including women of childbearing age, are exposed to phthalates in medications.

Estimating associations with male genital malformations

The next step was to investigate the association between exposure to phthalates in medications during pregnancy and male genital malformations, such as hypospadias and cryptorchidism, in offspring, using the Slone Epidemiology Center Birth Defects Study.

From defining the exposure, to estimating associations with health outcomes, Hernandez-Diaz's research on phthalates in medications illustrates the innovative and collaborative process that drives environmental health research.



Hernandez-Diaz described her research on medications containing phthalates as a story with many chapters, which included identifying medications with phthalates; exploring the exposure burden in the U.S. population, specifically among pregnant women; and estimating associations between medications containing phthalates and male genital malformations in offspring. (Photo courtesy of Steve McCaw)

“This story is an example of how things can happen in epidemiology and be fun and interesting when you have collaboration among scientists with different expertise,” Hernandez-Diaz said.

(Annah Wyss, Ph.D., is an Intramural Research Training Award postdoctoral fellow with the NIEHS Genetics, Environment, and Respiratory Disease Group.)

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New exposure biomarkers enhance breast cancer research

By Kimberly Cannady

Researchers from the Silent Spring Institute in Newton, Massachusetts, which is funded in part by NIEHS, published a study that is the first to comprehensively examine chemicals linked to breast cancer risk and recommend methods for their detection. The [study](#) was published in the May issue of the journal *Environmental Health Perspectives*.

Scientists examined chemical carcinogenicity studies in rodents, to extend the scope of breast cancer epidemiology in humans. According to the study authors, the limited understanding of the biological pathways involved in breast cancer development has impeded the ability of scientists to anticipate which chemicals may increase risk. The use of animal studies provides a basis for anticipating the effects of these chemicals in humans.

“The study provides a road map for breast cancer prevention by identifying high-priority chemicals that women are most commonly exposed to and demonstrates how to measure exposure,” said lead author [Ruthann Rudel](#), director of research at the Silent Spring Institute. “This information will guide efforts to reduce exposure to chemicals linked to breast cancer and help researchers study how women are being affected.”



Rudel leads the exposure and toxicology research programs at the Silent Spring Institute. (Photo courtesy of Jessica Helm)

Chemical selection and methods to measure exposure

Previously, Rudel and colleagues identified 216 chemicals as potential breast cancer carcinogens, because they caused cancer in rodent studies. After a systematic review of chemical use, exposure, and toxicology data, they narrowed the list down to 102 mammary carcinogens that have high occupational exposure rates, are produced in high volumes, or are present in food, polluted air, and consumer products.

Seventy-five of them fell into 17 groups, based on common exposure potential or structural similarity. These chemicals are found in gasoline fumes, cigarette smoke, diesel exhaust, polyurethane foams and sealants, flame retardants, nonstick and stain-resistant coatings, paint removers, and byproducts of drinking water disinfection.

“Every woman in America has been exposed to chemicals that may increase her risk of getting breast cancer,” said co-author [Julia Brody, Ph.D.](#), executive director of the Silent Spring Institute.

In addition to compiling a list of potential human breast carcinogens, the researchers recommended methods used to measure the presence of these chemicals, termed exposure biomarkers, in women, based on experimental evidence. These include measuring the presence of the parent compound in blood, the metabolite in urine, and DNA and protein adducts, which are interactions of the parent or metabolite with the proteins or DNA.

Translating animal studies to human models

To demonstrate the relevance of rodent studies to humans, Rudel and colleagues also compared evidence in rodents and humans, for those agents that have been reasonably well-studied in humans. “It is biologically plausible that agents for which there is sufficient evidence of carcinogenicity in experimental animals also present a carcinogenic hazard to humans,” according the International Agency for Research on Cancer in a [Silent Spring Institute press release](#).

The new study also identified 44 cohort studies, with a total of more than 3.5 million women enrolled, that have recorded breast cancer incidence and stored blood or urine samples. These additional biomarker measurements can be incorporated into the current study to further evaluate breast cancer risk associated with chemical exposures.

Dale Sandler, Ph.D., chief of the NIEHS [Epidemiology Branch](#), believes this study will be of great use. “This paper is a thorough review of toxicology data and biomarkers relevant to breast cancer in humans,” Sandler said. “It is a terrific resource for epidemiologists thinking about studying environmental contributors to breast cancer.”

Citation: [Rudel RA](#), [Ackerman JM](#), [Attfield KR](#), [Brody JG](#). 2014. New exposure biomarkers as tools for breast cancer epidemiology, biomonitoring, and prevention: a systematic approach based on animal evidence. *Environ Health Perspect*; doi:10.1289/ehp.1307455 [Online 12 May 2014].

(Kimberly Cannady, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Chromatin and Gene Expression Group.)

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Brody's research is focused on the effects of the environment on breast cancer. (Photo courtesy of Dan Brody)

Novel integrative approach sheds light on embryonic stem cell identity

By Simone Otto

Just as every human has a unique personality, every cell type expresses a unique set of proteins necessary to its identity. In a new study published in the April issue of the journal *Proceedings of the National Academy of Sciences*, researchers at NIEHS reported a novel computational approach to identify genes associated with embryonic stem cell (ESC) identity

Senthilkumar Cinghu, Ph.D., visiting fellow in the NIEHS Systems Biology Group (SBG), is lead author of the [study](#). “Identification and characterization of genes that maintain ESC identity is a key first step toward using ESCs as models for stem cell transplantation therapies and toxicity tests,” he said.

Illuminating ESC regulation

ESCs are pluripotent, meaning they have the power to become any cell in the adult human body. During development, ESCs must be able to divide rapidly and repeatedly without acquiring mutations associated with oxidative stress, as happens in adult cells. According to the authors, this research illuminates a novel regulatory mechanism that facilitates rapid proliferation of ESCs without compromising genomic stability.

“Ever-increasing evidence, supporting the possible hijacking of stem cell self-renewal pathways by cancer stem cells, makes it all the more important to identify, characterize, and understand the pathways that control ES cell identity,” said **Raja Jothi, Ph.D.**, lead researcher on the study and head of SBG.

Assigning ranks to genes

Sailu Yellaboina, Ph.D., former visiting fellow in SGB, led the effort to develop a computational approach for systematic integration of published gene expression data, to rank-order genes based on their likelihood of defining a cell type of interest. This approach favors genes that are consistently reported in many studies to be highly expressed in ESCs — the cell type of interest in this study — and significantly down-regulated during the normal course of ESC differentiation.

“You’re basically leveraging the evidence from a number of data sets and the consistency of data sets to make a reasonably good set of predictions,” explained Jothi.

Many genes ranked as most important to determining ESC identity were also members of protein complexes known to be important in ESCs, whereas genes from complexes known to be important for cell differentiation ranked near the bottom of the order.

Nucleolin is an important shield against oxidative stress

The most exciting result was the unexpectedly high rankings of many genes that had never been implicated in ESC biology. **Guang Hu, Ph.D.**, head of the NIEHS Stem Cell Biology Group, joined forces with Jothi and his team to validate over a dozen novel ESC regulators, including Nucleolin, a gene whose expression is particularly high in cancer cells. The researchers revealed the



“Given that ES cells and cancer stem cells have similar phenotypic traits, the novel Nucleolin-dependent bistable switch we report in ESC cells [see image below] paves the way for the development of new drug targets for cancer therapy,” said Cinghu. (Photo courtesy of Steve McCaw)



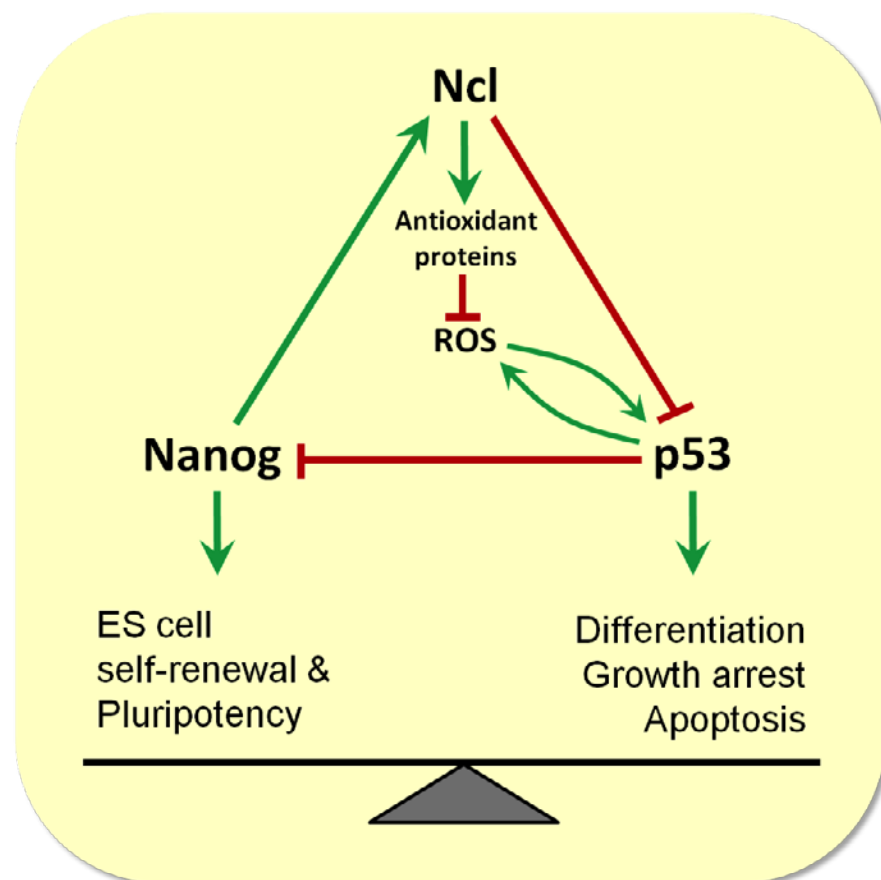
“ESCs are an excellent model for developing new therapies toward regenerative medicine, as well as testing new drugs, especially when there is no good animal model for the disease being studied. Any progress in these areas requires identification and characterization of key genes regulating the homeostatic balance between self-renewal and differentiation in ES cells,” said Jothi. (Photo courtesy of Steve McCaw)

essential role of Nucleolin in ESC homeostasis, for its role in shielding against oxidative stress induced by redox imbalance, which can induce ESC differentiation (see image below).

“Given the similarities between ESCs and cancer cells, we expect our findings to set the stage for understanding not only tumorigenesis, but also cell fate decisions in cancer stem cells, which are widely believed to possess tumor-initiating capabilities,” Jothi said.

Citation: Cinghu S, Yellaboina S, Freudenberg JM, Ghosh S, Zheng X, Oldfield AJ, Lackford BL, Zaykin DV, Hu G, Jothi R. 2014. Integrative framework for identification of key cell identity genes uncovers determinants of ES cell identity and homeostasis. *Proc Natl Acad Sci U S A* 111(16):E1581-E1590.

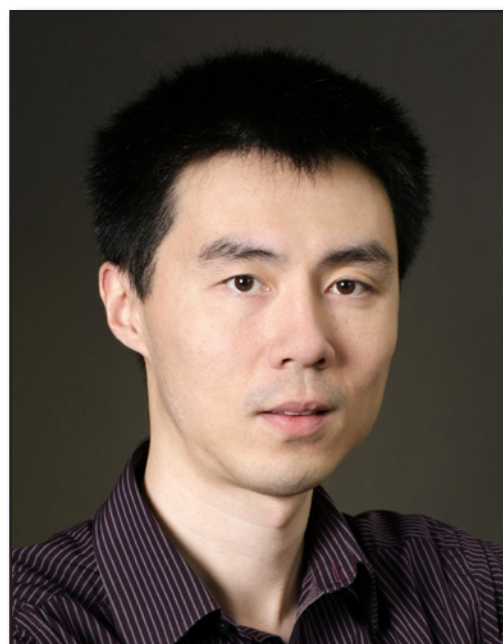
(Simone Otto, Ph.D., is an Intramural Research and Training Award fellow in the NIEHS Ion Physiology Channel Group.)



Proposed model for Nucleolin (Ncl)-mediated regulation of the homeostatic balance between self-renewal and differentiation in ESCs, called an Ncl-dependent Nanog-p53 bistable switch. The balance may be disturbed by depletion of Ncl, leading to reactive oxygen species (ROS)-induced p53 activation and subsequent self-renewal defects and differentiation. The transcriptional regulation of Ncl by Nanog, a master ESC regulator protein, restrains p53, which, when activated, suppresses Nanog. This reciprocity may control the homeostatic balance between ESC self-renewal and cell differentiation. (Image from Cinghu et al. 2014)



Yellaboina, an equal contributor with Cinghu in the study, recently left NIEHS to become an associate professor at the C.R. Rao Advanced Institute of Mathematics, Statistics, and Computer Science at the University of Hyderabad in India. (Photo courtesy of Steve McCaw)



The research of Hu and his group seeks to facilitate the development of stem cell therapies, and contribute to understanding how environmental factors can affect human embryogenesis and early development. (Photo courtesy of Steve McCaw)

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Yao receives award and helps launch new center

By Eddy Ball

NIEHS lead researcher Humphrey Yao, Ph.D., was in Denmark last month, participating in the launch of a new research center May 15, and delivering presentations May 16 at the 18th European Testis Workshop ([ETW18](#)). Both events reflected the increasing interest in male reproductive development, and the effects of endocrine disruption on human health.

Yao heads the NIEHS Reproductive Developmental Biology Group, which studies the normal process of the formation of gonads and reproductive tracts during the early stages of prenatal development, and investigates whether this process is susceptible to *in utero* exposure to endocrine disruptors.

As a first of its kind, the new International Center for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health ([EDMaRC](#)) will support multidisciplinary research led by internationally recognized scientists. EDMaRC is located in the Department of Growth and Reproduction at Rigshospitalet in Copenhagen, in close collaboration with the University of Copenhagen.

While at ETW18 in Elsinor, Yao gave two talks — “Autocrine/Paracrine Regulation of Sertoli Cell Identity in Fetal Mouse Testis” and “Hedgehog in the Testis: Its Role in Origins and Differentiation of Leydig Cells.” Following his presentations, Yao was recognized as best speaker among the 21 plenary speakers at the workshop by the [International Network for Young Researchers in Male Fertility](#).



Yao is the recipient of the Basal O'Connor Starter Scholar Research Award from March of Dimes Foundation, Pfizer Research Award, New Investigator Award from the Society for the Study of Reproduction, and Young Andrologist Award from the American Society of Andrology. (Photo courtesy of Steve McCaw)

An epidemic of male reproductive disorders

As Yao explained, ETW and EDMaRC are both dedicated to addressing disturbing trends in male reproductive health worldwide. “Danish researchers were among the first to publish a very famous hypothesis on testicular dysgenesis [abnormal development] syndrome,” he said.

Detailed medical records for young men drafted in northern European countries document a steady increase over the past 30 years of poor sperm quality, undescended testes, testicular cancer, and hypospadias, or congenital defects in the opening of the penis. Researchers increasingly believe that these disorders may, in large part, be due to exposure to endocrine disrupting chemicals in the environment.

ETW18 is part of a series of conferences, founded in 1980, that rotate between Europe and the U.S., helping to raise awareness of male reproductive disorders. Research interest is strong in Denmark, especially in Copenhagen, where the Department of Growth and Reproduction at Rigshospitalet has been a global leader in the field. ETW18 attracted 162 scientists from 28 countries.

The program for the launch of EDMaRC included a statement of support from NIEHS and NTP Director Linda Birnbaum, Ph.D. “There is a great need for more research and training on the role of the environment and health, especially in the areas of disruptors and male reproduction ... through a center specifically set up to integrate research across the spectrum,” she wrote.

“The Department of Growth and Reproduction [in Copenhagen] is not only internationally recognized as a leading center of research on the role of environment in male reproduction, but [it] also has the structure, expertise, and location that makes it the perfect setting for this type of translational research,” she concluded.

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This month in EHP

The June issue of Environmental Health Perspectives (EHP) examines potentially harmful exposures from cooking, especially when using gas stoves, and the benefits seen in Denmark after the country reduced antibiotic use in livestock.

Take Care in the Kitchen: Avoiding Cooking-Related Pollutants —

The process of cooking food, as well as the stoves themselves — especially gas burners — can emit several potentially hazardous chemicals and compounds. Researchers suggest a few simple techniques to reduce exposure while they look for better ways to control emissions.

Reducing Antibiotic Use in Livestock: How Denmark Tackled

Resistance — In Denmark, the drive to preserve antibiotics for human use revolutionized livestock management during the 1990s and 2000s. Today the country is enjoying a thriving livestock industry and a decrease in antibiotic-resistant microbes in animals and meat.

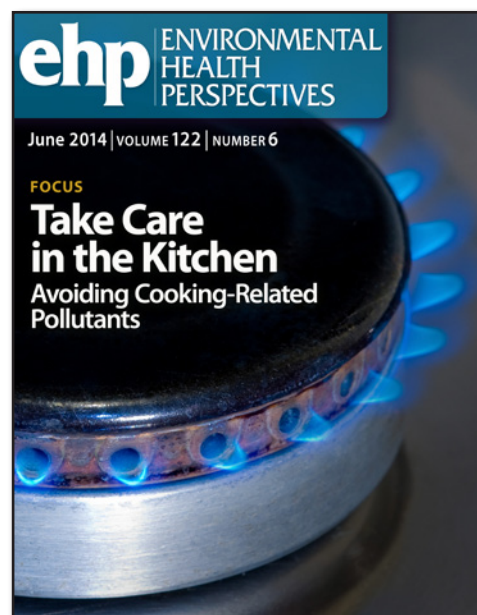
Featured research and related news articles this month include:

- **Assessment of the Risk of Medium-Term Internal Contamination in Minamisoma City, Fukushima, Japan, after the Fukushima Daiichi Nuclear Accident** — Data for Disaster Planning: Risk Factors for Internal Radiation Exposures After Fukushima
- **Ciguatera Fish Poisoning and Climate Change: Analysis of National Poison Center Data in the United States, 2001–2011** — Under the Weather With Ciguatera Fish Poisoning: Climate Variables Associated With Increases in Suspected Cases
- **Estimated Effects of Projected Climate Change on the Basic Reproductive Number of the Lyme Disease Vector *Ixodes scapularis*** — Ticking Time Bomb? Climate Change and *Ixodes scapularis*
- **The Human Early-Life Exposome (HELIX): Project Rationale and Design** — The HELIX Project: Tracking the Exposome in Real Time

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Extramural papers of the month

By *Nancy Lamontagne*

- [Olestra reduces PCBs in the body](#)
- [Activation and regulation of polymerase V during DNA synthesis](#)
- [SSRI use during pregnancy associated with autism](#)
- [Coal-burning stoves in Mongolia linked to seasonal variance in miscarriages](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

Olestra reduces PCBs in the body

According to a study funded in part by NIEHS, the zero-calorie fat substitute olestra can speed the removal of polychlorinated biphenyls (PCBs) from the body. The findings suggest that olestra could offer a low-risk dietary intervention for people exposed to PCBs.

Olestra is a nonabsorbable fat substitute introduced in snack foods in 1996. Animal studies have suggested that olestra could increase the rate that organochlorines, such as PCBs, are cleared from the body. The researchers tested its effectiveness in 28 people with high levels of PCBs. All of them lived in Anniston, Alabama, site of a plant that manufactured PCBs for 40 years.

During the yearlong study, half of the participants consumed, per day, 12 Pringles brand potato chips made with vegetable oil, and the other half consumed, per day, 24 Pringles made with olestra. Total daily intake of olestra was 15 grams. The serving sizes were different, to help equalize calorie consumption between the test groups. Overall, the rate of PCB clearance from the participants who ate the chips made with olestra was faster during the one-year trial than before the trial. Two participants in the olestra group showed a decrease in concentration of PCBs of 27 percent and 25 percent during the trial. The researchers suggest that olestra apparently makes fat-soluble compounds, like PCBs in the intestine, more likely to be dissolved, reducing absorption of these compounds into the body.

Citation: Jandacek RJ, Heubi JE, Buckley DD, Khoury JC, Turner WE, Sjodin A, Olson JR, Shelton C, Helms K, Bailey TD, Carter S, Tso P, Pavuk M. 2014. Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial. *J Nutr Biochem* 25(4):483-488.

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Activation and regulation of polymerase V during DNA synthesis

When a cell's DNA replication machinery reaches damaged DNA, it must either repair or bypass the damage to copy its genome. In *E. coli*, the enzyme polymerase V can copy past damaged DNA, but it often introduces new mistakes when copying undamaged DNA. NIEHS grantees have discovered new details about the molecular basis for polymerase V activation, and a unique regulatory mechanism that limits polymerase V synthesis to the short DNA segments where it is needed. Understanding the role of DNA polymerases, in either inducing or preventing mutations, will have wide-ranging implications for understanding disease initiation or progression, and individual susceptibility, as well as determining treatment and prevention strategies.

The investigators used biochemical techniques to better understand how binding to the RecA protein and adenosine triphosphate (ATP) activates polymerase V. They found that the enzyme must bind to an ATP molecule before attaching to the DNA, and it must remain bound to ATP during DNA synthesis. The enzyme then breaks down the molecule of ATP to free itself from the DNA. Although the RecA protein can also break down ATP, the researchers found that mutant RecA lacking this ability can still trigger DNA polymerase V to break down ATP itself.

No DNA polymerase has been observed to be regulated by ATP in this way. According to the researchers, this extra control would limit DNA polymerase V to only copying damaged DNA, and keep it from copying neighboring stretches of undamaged DNA where it would likely introduce new errors.

Citation: [Erdem AL, Jaszczur M, Bertram JG, Woodgate R, Cox MM, Goodman MF](#). 2014. DNA polymerase V activity is autoregulated by a novel intrinsic DNA-dependent ATPase. *eLife* 3:e02384.

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SSRI use during pregnancy associated with autism

New results from the NIEHS-funded Childhood Autism Risks from Genetics and the Environment (CHARGE) study show an association between prenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and autism spectrum disorder, as well as developmental delays in boys. SSRIs are a frequently prescribed treatment for depression, anxiety, and other disorders.

The researchers examined 966 mother-child pairs participating in the CHARGE study and found that prenatal SSRI exposure was nearly three times as likely in boys with autism spectrum disorder, compared to boys with typical development, with the greatest risk occurring if exposure took place during the first trimester. SSRI use was also elevated among boys with developmental delays, with the strongest exposure effect in the third trimester.

The researchers acknowledge limitations of the study, including the difficulty of isolating SSRI effects from those of their indications for use, as well as the relatively small sample of children with developmental delays. They also note that because maternal depression also carries risks for the fetus, the benefits of prenatal SSRI use should be carefully weighed against potential risks.

Citation: [Harrington RA, Lee LC, Crum RM, Zimmerman AW, Hertz-Picciotto I](#). 2014. Prenatal SSRI use and offspring with autism spectrum disorder or developmental delay. *Pediatrics* 133(5):e1241-e1248.

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Coal-burning stoves in Mongolia linked to seasonal variance in miscarriages

According to research funded by NIEHS, pollution from the coal-burning stoves used in Ulaanbaatar, Mongolia, for winter heating, is strongly associated with miscarriages. Ulaanbaatar is the coldest capital city in the world, and one of the most air polluted.

To examine the association between miscarriages and seasonal variation of air pollutants, the investigators used measurements from Mongolian Government Air Quality Monitoring stations, and medical records of 1,219 women admitted to the hospital due to miscarriage. The overall rate of miscarriage reported in Ulaanbaatar was similar to that of Western countries, but miscarriages, per calendar month, increased from 23 per 1,000 live births in May 2011 to 73 per 1,000 live births in December 2011. Monthly average ambient levels of air pollutants increased in relation to hours of darkness and coldest temperatures, when the coal heating stoves are used most. Regression analysis of ambient pollutants against fetal death revealed dose-response correlations for sulfide dioxide $r > 0.9$ ($p < 0.001$), nitrogen dioxide ($r > 0.8$), carbon monoxide ($r > 0.9$), PM 10 ($r > 0.9$) and PM 2.5 ($r > 0.8$), ($p < 0.001$), indicating a strong correlation between air pollution and decreased fetal wellbeing.

Although major policy changes are helping to curb air pollution in Mongolia, the researchers speculate that up to five-fold further reduction in air pollutants in winter would be needed, to reduce fetal death rates to levels experienced during the summer in Ulaanbaatar.

Citation: [Enkhmaa D, Warburton N, Javzandulam B, Uyanga J, Khishigsuren Y, Lodoysamba S, Enkhtur S, Warburton D. 2014. Seasonal ambient air pollution correlates strongly with spontaneous abortion in Mongolia. BMC Pregnancy Childbirth 14\(1\):146.](#)

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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Intramural papers of the month

By Suchandra Bhattacharjee, Raj Gosavi, Gabriel Knudsen, Shannon Whirledge, and Annah Wyss

- [NTP researchers find potential treatment for damaged salivary glands is safe and effective](#)
- [Human obesity increases colon cancer risk](#)
- [New computational approach identifies essential stem cell genes](#)
- [p53 and NF-kappaB work together to promote inflammation](#)
- [More evidence for smoking-related changes in DNA methylation](#)

NTP researchers find potential treatment for damaged salivary glands is safe and effective

Researchers from NTP and the National Institute of Dental and Craniofacial Research have demonstrated that an adeno-associated virus (AAV) that contains the human aquaporin-1 gene (hAQP1) may be used to treat salivary gland dysfunction. The hAQP1-encoded protein is a molecular water channel that promotes the rapid movement of water in or out of a cell. Since patients with head and neck cancers often experience irreversible salivary gland damage as a result of radiation therapy, the new strategy may offer a way to prevent the conditions that arise in these patients, such as dry mouth, oral infections, and difficulty swallowing.

In a previous small-scale clinical trial, involving 11 patients with damaged salivary glands, researchers delivered adenoviral vector encoding hAQP1, which resulted in increased salivary flow in 5 patients. However, the gains were short-lived. The research team then evaluated a serotype 2 recombinant AAV encoding AQP1 (rAAV2hAQP1).

The scientists delivered increasing concentrations of rAAV2hAQP1 directly to impaired parotid glands in mice. The procedure caused mild local inflammation, but the vector remained localized to the ducts. Proper salivary gland function was restored and no significant adverse effects were noted in clinical chemistry or histopathology evaluations, indicating the treatment is clinically safe. Submission for a clinical trial is underway. **(GK)**

Citation: Momot D, Zheng C, Yin H, Elbekai RH, Vallant M, Chiorini JA. 2014. Toxicity and biodistribution of the serotype 2 recombinant adeno-associated viral vector, encoding Aquaporin-1, after retroductal delivery to a single mouse parotid gland. PLoS One 9(3):e92832

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Human obesity increases colon cancer risk

A research team, led by NIEHS scientists, determined that obesity, rather than diet, causes changes in the colon that may lead to colorectal cancer. The work provides support to the belief that calorie control and frequent exercise are keys to lowering risk.

The researchers used two groups of mice. The first contained a human version of the gene NAG-1, which protects against colon cancer, and the second lacked this gene. Both groups were fed a high-fat diet. The scientists determined that the NAG-1 group did not gain weight, while the second group grew plump. After studying histone acetylation patterns in isolated colon cells, team members found that the acetylation patterns in the obese group resembled patterns from mice that had colorectal cancer. The additional weight carried by this group also activated genes that helped promote the rapid progression of cancer.

The findings suggest that preexisting colon lesions in obese individuals are more likely to rapidly evolve into malignant tumors. The group is working to identify signaling pathways, which may help scientists find ways to treat colorectal cancer in obese patients. **(SB)**

Citation: Li R, Grimm SA, Chrysovergis K, Kosak K, Wang X, Du Y, Burkholder A, Janardhan K, Mav D, Shah R, Eling TE, Wade PA. 2014. Obesity, rather than diet, drives epigenomic alterations in colonic epithelium resembling cancer progression. Cell Metab 19(4):702-711. [[Story](#)]

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New computational approach identifies essential stem cell genes

NIEHS researchers have developed a computational approach to systematically integrate published gene expression data to identify genes that define a cell's identity. The approach, which was validated in an article that appeared in the journal PNAS, identified genes with essential roles in embryonic stem cell (ESC) maintenance and cell fate decisions in cancer.

Although genetic screens have implicated more than 400 genes in ESC maintenance, these screens have limited overlap, and secondary validation remains a costly and time-consuming alternative. To preselect and prioritize candidate genes, the authors developed a bioinformatics framework to rank-order genes based on gene expression data from 68 experiments profiling undifferentiated ESCs and various differentiated cell types. The effectiveness of the approach was evident from the enrichment of well-characterized ESC regulators, including Oct4, Nanog, and Sox2. Furthermore, the authors uncovered many novel ESC maintenance genes, including Nucleolin, which they report, for the first time, as a key upstream regulator of Nanog.

The authors believe that the utility of their computational approach to identifying ESC gene regulators reaches beyond understanding basic ESC biology. Many parallels exist between ESC self-renewal and tumorigenesis. Identifying and understanding the gene networks that are associated with traits found in both ESCs and cancer will likely enhance scientists' understanding of tumor initiation. **(SW)**

Citation: [Cinghu S, Yellaboina S, Freudenberg JM, Ghosh S, Zheng X, Oldfield AJ, Lackford BL, Zaykin DV, Hu G, Jothi R.](#) 2014. Integrative framework for identification of key cell identity genes uncovers determinants of ES cell identity and homeostasis. *Proc Natl Acad Sci U S A* 111(16):E1581-1590. [[Story](#)]

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p53 and NF-kappaB work together to promote inflammation

Scientists at NIEHS and the University of North Carolina at Chapel Hill reported that the tumor suppressor p53, and the transcriptional regulator nuclear factor-kappaB (NF-kappaB), work together in human macrophages to induce inflammation. The study, which was published in the journal *Cancer Research*, suggests that pharmaceutical compounds designed to block this interaction could help treat the inflammation many cancer patients experience during chemotherapy.

The study compared expression levels of cytokines and chemokines in macrophages from healthy humans and tumor-conditioned macrophages. The authors observed increased expression of proinflammatory genes, interleukin 6 (IL-6), and chemokine (C-X-C motif) ligand 1 (CXCL1), in the macrophages, when p53 was activated by chemotherapeutic drugs. They noted that NF-kappaB coactivation is essential for upregulation of these genes.

The authors also showed a role for p53 in tumor-associated macrophages (TAMs). In the tumor microenvironment, macrophages are programmed to produce proinflammatory proteins, such as IL-6, which promote tumorigenesis. They found that p53 is activated in TAM-like cells, facilitating the production of IL-6. This discovery reveals that p53 may have significant functions in carcinogenesis outside of its well-described function as a tumor suppressor, which could have important implications in tumor progression and tumor responses to chemotherapy. **(RG)**

Citation: [Lowe JM, Menendez D, Bushel PR, Shatz M, Kirk EL, Troester MS, Garantzotis S, Fessler MB, Resnick MA.](#) 2014. p53 and NF-kappaB coregulate proinflammatory gene responses in human macrophages. *Cancer Res* 74(8):2182-2192. [[Story](#)]

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More evidence for smoking-related changes in DNA methylation

In a paper published in April, NIEHS scientists reported altered DNA methylation in relation to cigarette smoking in adult women. The work both validated 10 CpG sites that had been previously identified and discovered smoking associations at 2 new CpG sites. These discoveries may help identify the epigenetic pathways by which smoking leads to a variety of adverse health outcomes.

The scientists utilized data from the Sister Study, a prospective cohort study of women designed to identify the environmental and genetic causes of breast cancer. Team members examined the relationship between smoking and methylation using two epigenetic datasets: one that had methylation array data on 27,578 CpG sites for each of 908 women, and one that had methylation array data on 473,844 CpG sites for each of 200 women. In addition, they validated their primary findings using pyrosequencing. Notably, one of the new sites they identified was in a gene responsible for heme synthesis, the molecule that carries oxygen in blood. This work helps to extend the findings that cigarette smoking and other environmental exposures are associated with persistent epigenetic modifications to DNA. **(AW)**

Citation: [Harlid S, Xu Z, Panduri V, Sandler DP, Taylor JA](#). 2014. CpG sites associated with cigarette smoking: analysis of epigenome-wide data from the Sister Study. *Environ Health Perspect*; doi:10.1289/ehp.1307480 [Online 4 April 2014].

(Suchandra Bhattacharjee, Ph.D., is a special volunteer in the NIEHS Free Radical Metabolism Group. Raj Gosavi, Ph.D., is a research fellow in the NIEHS Structure and Function Research Group. Gabriel Knudsen, Ph.D., is a Intramural Research Training Award fellow in the National Cancer Institute Center for Cancer Research Laboratory of Toxicology and Toxicokinetics. Shannon Whirlledge, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Molecular Endocrinology Group. Annah Wyss, Ph.D., is an IRTA fellow with the NIEHS Genetics, Environment, and Respiratory Disease Group.)

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Inside the Institute

Administrative professionals recharge and empower at NIEHS seminar

By Kelly Lenox

In celebration of Administrative Professionals Day, the NIEHS Office of Management honored clerical, administrative, secretarial, and technical staff during an April 23 event. The day began with a seminar, “Recharge and Empower Yourself as an Administrative Professional,” by Sallie Dewar of the Human Resources Institute in Maryland.

Joellen Austin, NIEHS associate director for management, opened the event by sharing her memories of Secretary’s Day, as it was called in the past, and introducing Dewar.

Recognizing accomplishments

Dewar began by asking participants to collect in small groups and review their accomplishments together. Each team then shared each other’s accomplishments with the whole group. Stories ranged from the personal, like helping children succeed in middle school or earning a masters degree while working full time, to the professional, such as completing budget closeouts and planning international travel.

Dewar commented on how difficult it can be to come up with a list of accomplishments. “I’ll bet you don’t realize the impact you have in the organization,” she said. “Most people won’t be aware of what you do on a daily basis, until you share it with them.”

Participation in these group presentations energized the attendees. According to Robbie Majors, administrative support in the NIEHS Genes, Environment, and Health Branch, that was an unusual, and important, part of the program. “We need experience talking in front of people,” Majors said. “We know what’s going on, and we need more opportunities to get up and answer questions.”

Talking your way out of stress

According to Dewar, stress is a major epidemic, affecting people in all walks of life. “If you don’t control stress, stress will control you,” she said. Referring to the presentations they’d just made, one participant identified public speaking as a source of stress, generating agreement and hearty laughter across the room.

Dewar sought concrete strategies from participants, engaging even the shyest among the group. Suggestions ranged from walking away from the desk for a few minutes, to fishing and recreation, to writing and other creative outlets. Dewar also offered approaches aimed at altering the work environment, such as clarifying expectations with co-workers, making requests clear, and developing a sense of a working partnership with supervisors.



Dewar underscored her message on the importance of respect by individually greeting participants as they arrived. She offered techniques to stay focused and positive, even in difficult situations; create winning partnerships with supervisors; and receive recognition for the important and hard work administrative professionals do all year long. (Photo courtesy of Steve McCaw)

“R-E-S-P-E-C-T — find out what it means to me”

According to Dewar, earning and being treated with respect goes a long way toward relieving workplace stress. Quoting Aretha Franklin, Dewar noted that respect might look different to different people.

She urged participants to have discussions about respect, continuing her theme of focusing on actions that lie within each person’s capabilities. Dewar left the group with plenty of food for thought. “What do you want to be known for?” she asked.

Celebration

The day ended with a cake and ice cream social, hosted by NIEHS leadership, giving them the opportunity to personally thank the administrative professionals for their hard work and dedication during the year.



After introducing Dewar, Austin participated in the workshop, as did other members of the management team. (Photo courtesy of Steve McCaw)



Valarie Sims, left, and David Kinnamont enjoyed a lighthearted discussion. (Photo courtesy of Steve McCaw)



From left, Marsha Johnston, Cindy Gerrard, and Kristen Fisher discussed their group presentation during the workshop session. (Photo courtesy of Steve McCaw)



From left, Pinkney Wilder, William Boyd, and Ed Kang took turns sharing each other’s achievements, with no shortage of humor. (Photo courtesy of Steve McCaw)



Majors, center, shown with group members Diana Callender, right, and Rosemary Moody, appreciated the public speaking opportunity. “It was a good experience, and it was entertaining, too,” Majors said, referring to the laughter and applause that many of the presentations generated. (Photo courtesy of Steve McCaw)

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NIEHS renovation team wins HHS Green Champions Award

By Kelly Lenox

A recent renovation in building 101, also known as the Rall Building, on the NIEHS campus in Research Triangle Park, North Carolina, attracted some well-deserved attention from the U.S. Department of Health and Human Services (HHS).

Each year, HHS presents Green Champions Awards to individuals and groups who dramatically reduce greenhouse gas emission, energy and water consumption, and pollution, through projects within their organizations. This year, an award was given to a team from NIEHS, during a June 13 ceremony at the National Institutes of Health in Bethesda, Maryland.

The Green and Fit Retrofit Team, led by Debra Del Corral and Amanda Thompson of the NIEHS Office of Management, and Joseph Seufert III of the NIH Office of Research Facilities (ORF), won the Sustainable Design and Facilities Award, given in recognition of exceptional efforts toward sustainability.

“The entire team deserves recognition for winning,” said Seufert, noting the strong support received from NIH ORF Engineering, Maintenance, and Operations; the NIEHS Office of Acquisitions; NIEHS end users; and many contractors.

A model green renovation project

The team focused on using repurposed, recycled, and reclaimed building materials in the remodel, which provided improved facilities for fitness, work-life balance, training, the library, and the Integrative Bioinformatics team (see [story](#)).

The Green Champions Award recognizes the exemplary use of green design and building materials in the renovation effort. “Throughout the project, building materials were reused; furnishings were refurbished and reinstalled; metal materials were recovered and recycled; healthy paints, adhesives, and finishes were applied; energy-efficient lighting and heating/cooling systems were installed; and water conserving fixtures were built in,” wrote the HHS committee that selected the winners.

The award notice pointed to financial, workplace quality, scientific support, and health gains. “The Institute improved its ability to meet its emerging scientific mission in bioinformatics and scientific training, and saved hundreds of thousands of dollars. At the same time, NIEHS kept tons of material out of landfills, installed healthy and efficient materials and engineering systems, and promoted employee fitness and quality of life.”

In an Institute dedicated to supporting environmental public health, this team’s work stands as a model for other NIH projects. NIEHS and NTP Director Linda Birnbaum, Ph.D., wasted no time in congratulating the team. “I am so proud of the ways in which these award winners have contributed to the NIEHS mission and exemplify stewardship of our resources,” she said.



According to the award committee, the efforts of Green and Fit Retrofit Team, from left, Del Corral, Seufert, and Thompson, helped cut overall construction costs by 30-40 percent by eliminating multiple project phases. Other efficiencies saved at least \$160,000, and the project improved space utilization by eliminating passageways and optimizing layouts. (Photo courtesy of Steve McCaw)

Lead design architect revisits NIEHS

By Eddy Ball

More than three decades after completion of the main building at NIEHS, lead design architect Richard Banks returned to NIEHS May 19, for the first time since its completion, to see how his brainchild has flourished over the years.

NIEHS Special Assistant for Community Engagement and Outreach John Schelp organized the visit and hosted Banks and his family on a tour of the building and grounds.

Over lunch in the NIEHS cafeteria, Banks, his wife Marilyn, and son Erik talked with a small group of NIEHS employees about his concept for building 101, also known as the Rall building, and the support he enjoyed from former NIEHS Director David Rall, M.D., Ph.D., during design and construction of the project.

“He was a great champion of the design of this building,” Banks said. “He was behind it all the way.”

Lobbying for innovation

According to Banks, it was an uphill struggle to retain several elements that usually weren’t a part of government buildings at the time, especially the interstitial spaces between floors that give facilities staff access to utilities without disrupting work in the offices and labs above and below.

“The mandate was flexibility, and our response was a systems building, modular in concept, that optimized floor plan changes with a minimum of downtime,” he said. All the fixed service elements — fire stairs, elevators, and the main vertical mechanical shafts — are located outside the occupied spaces. The building’s aesthetic is a direct response to its function and environmental setting.

“We proved to them [our government contract officers] that it would be much more economical to do away with the corridors behind the labs and service them from above,” Banks said. “They were very skeptical about it..., [but] finally they came over to our side.”

The interstitial space wasn’t the only disagreement between Banks and contract officers at the Government Services Administration. The mall area that runs the entire length of the 334,000 square foot building also raised eyebrows in Washington, D.C., as did the striking copper laminate wall in the main lobby, and the exposed aggregate precast concrete panels used to clad the exterior.

Banks said he spent months analyzing the functions at NIEHS. His design team performed extensive life cycle cost analyses and value engineering studies throughout the entire design process. Among the innovations he introduced to the young institute were centralized glassware and media operations, and mail distribution, both located along the mall area. He argued for the mall and exterior designs, because he wanted the building to leave a lasting impression on occupants and visitors for years to come.



From left, Schelp joined Richard, Marilyn, and Erik Banks on the balcony outside the office of NIEHS and NTP Director Linda Birnbaum, Ph.D. As Banks scanned the landscape, he was able to see how his former firm’s master plan for the campus came to life. (Photo courtesy of Steve McCaw)

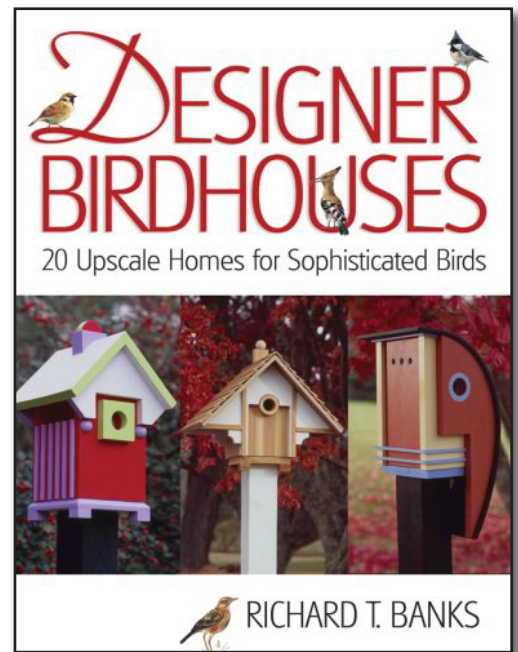
A satisfying look back

Following an award-winning, 40-year career that took him to major projects in Saudi Arabia, and saw him rise to president of Urbahn Associates, presently Urbahn Architects, his family moved to Pinehurst, North Carolina, just south of Raleigh, in 1996.

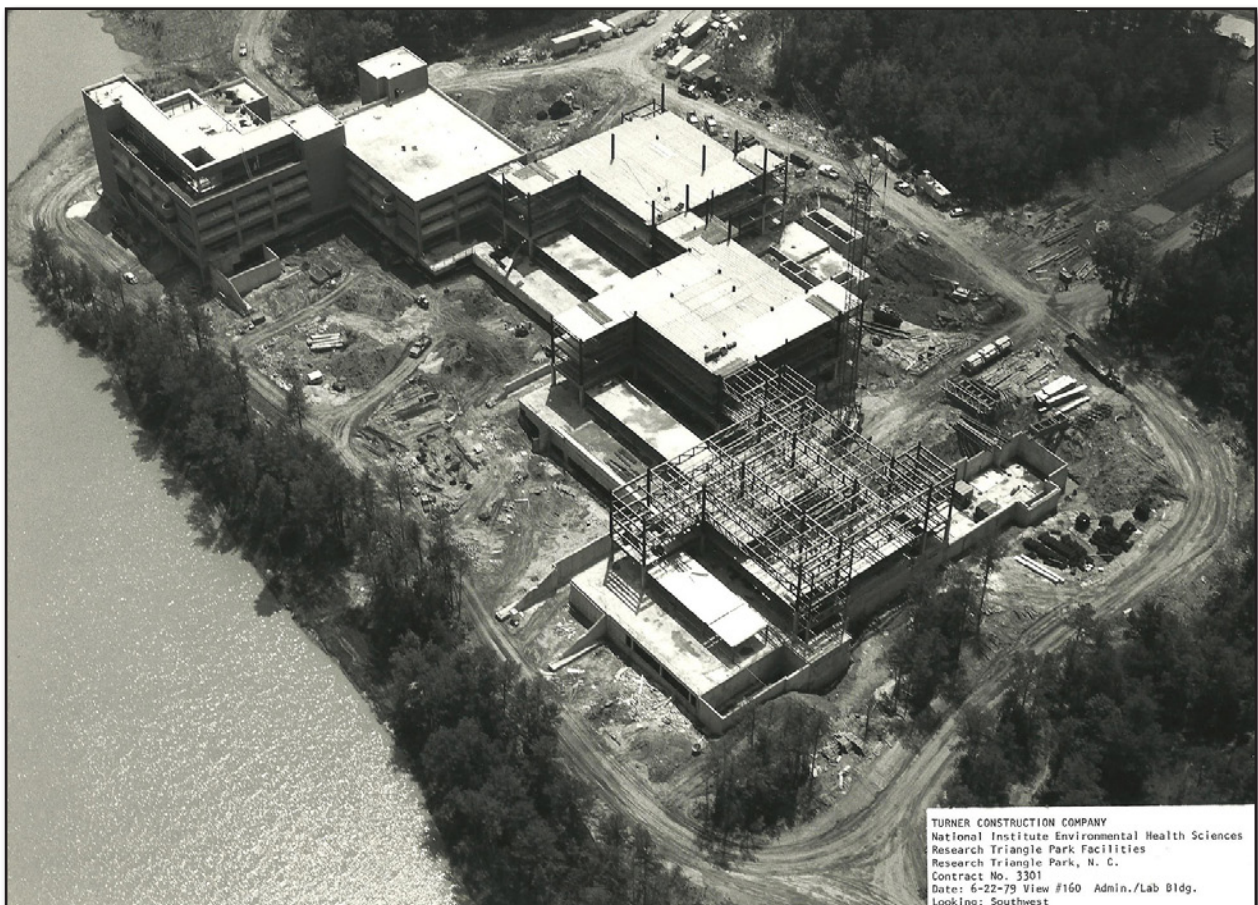
In his semiretirement, Banks pursues his passion for painting and still practices architecture, but on a specialized scale. His company, Richard T. Banks Architect, designs and builds intricately crafted birdhouses. In 2008, Lark Books published a book on his work, “Designer Birdhouses: 20 Upscale Homes for Sophisticated Birds.” He is currently working on books on aging and health, and the relationship between neuroscience and art.

Banks said he was gratified to see how well his creation has aged. When it was built, the NIEHS laboratory and administration building was so far ahead of its time that location scouts for Woody Allen’s science fiction parody “Sleeper” seriously considered it as a set for the film.

“For a building that’s [almost] 40 years old, I am shocked by how good a condition it’s in,” Banks said of his progeny. “Usually, you don’t find that in a government building.”



On a considerably smaller scale, Banks is still turning heads and winning praises with his designs. (Photo courtesy of Richard Banks)



By the summer of 1979, construction was well underway, and NIEHS employees looked forward to moving from the old North Campus into the new facility. (File photo courtesy of NIEHS)



Banks designed the building to work with the environment, a quality that has kept the building fresh more than three decades after its construction. (Photo courtesy of Steve McCaw)

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Fun and fitness abound during 2014 NIEHS Health and Fitness Week

By Ian Thomas

May 5 marked the beginning of NIEHS Health and Fitness Week, a fun-filled, five-day event held annually to promote exercise, nutrition, and all-around healthy living among Institute employees and contractors (see [sidebar](#)).

Widely considered by many at NIEHS as an unofficial rite of spring, this year's event brought with it the full slate of classic activities, such as the table tennis and 3-on-3 basketball, as well as a number of new ones, including Ultimate Frisbee and mental fitness Sudoku.

“Our goal each year is to provide fun, enticing, and health-related activities that promote functional lifestyles among everyone at NIEHS,” said Stephanie Bullock-Allen, contract program manager in the NIEHS fitness center, who noted the link between overall wellness and workplace productivity.



Contract scientist Jianying Li took aim in one of several table tennis events throughout the week. (Photo courtesy of Steve McCaw)

As always, the 2-mile nature walk and the Rogathon — a 5K run named for NIEHS epidemiologist Walter Rogan, M.D. — proved the biggest draw among participants. “I’ve been running this race off and on since 2000, and I always enjoy it,” said Jeff Tucker, biomedical engineer with the [NIEHS Calcium Regulation Group \(CRG\)](#) and first male runner across the finish line with a time of 21:05.

“I usually just run at the gym before work, so I wasn’t sure how I’d do on the road with hills,” said [Felicity Davis, Ph.D.](#), visiting fellow in CRG and the first female runner over the line at 25:03. “I had a lot of fun, though, and I’m glad I did it. Everyone did an amazing job organizing this event,” she said.

Health and Fitness Week takes place during National Physical Fitness and Sports Month, an observance designated by presidential proclamation. The fun-filled week is organized and coordinated by members of the NIEHS Office of Management, Health and Safety Branch, and Administrative Services and Analysis Branch.

(Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

2014 Health and Fitness Activities

Monday, May 5: Weekly challenges kickoff — take the stairs challenge, better-for-you bingo, mental fitness Sudoku, nutrition seminar, doubles table tennis tournament

Tuesday, May 6: Fitness assessments, international dance party, basketball shootout, cornhole competition, doubles table tennis tournament

Wednesday, May 7: Rogathon 5K and 2-mile nature walk, post-run walk stretch, self-defense session, 3-on-3 basketball round robin, doubles table tennis tournament

Thursday, May 8: Football throw, Ultimate Frisbee, pickleball, doubles table tennis tournament

Friday, May 9: Employee tennis outing (Morrisville Aquatic Center), employee golf outing (Lake Shore Golf Course)



[Wei Qu, Ph.D.](#), of the NTP Inorganic Toxicology Group, joined Li in another hard-fought match. (Photo courtesy of Steve McCaw)



This year's Rogathon runners took off on the 5K, as the whistle blew. (Photo courtesy of Steve McCaw)



Mike Resnick, Ph.D., head of the Chromosome Stability Group, celebrated another successful run in the 5K. (Photo courtesy of Steve McCaw)



Tucker, left, and Davis both turned in field-leading finishes. (Photo courtesy of Steve McCaw)



Linda Yu, biologist in the NIEHS Molecular Pathogenesis Group, showed off her moves at the international dance party. (Photo courtesy of Steve McCaw)



Greg Webb completed a long-range jump shot for the point. (Photo courtesy of Steve McCaw)



This year's international dance party proved to be a hit with NIEHS employees. (Photo courtesy of Steve McCaw)



From left, Greg Webb, Quentin Archie, and Mark Hambric of the Comparative Medicine Branch, completed a masterful comeback to win the 3-on-3 basketball round robin. (Photo courtesy of Steve McCaw)



From left, VeeVee Shropshire, Stephanie Bullock-Allen, and Lindia Engram recorded times and welcomed runners over the line at the Rogathon. (Photo courtesy of Steve McCaw)

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